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(54) Title: INHALATION MONITORING SYSTEM AND METHOD

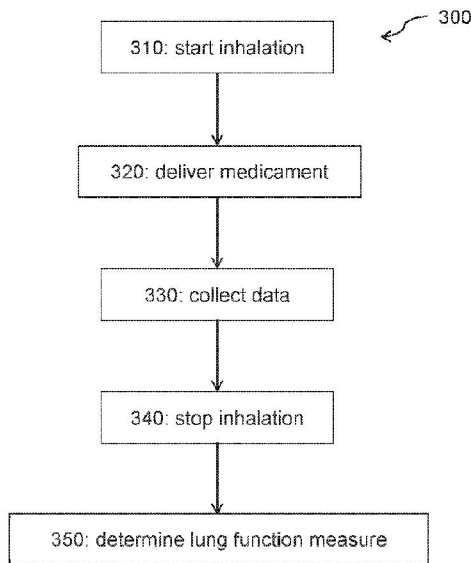


FIG. 3

(57) Abstract: An inhalation monitoring system includes an inhaler having a medicament delivery apparatus configured to deliver medicament to a user during an inhalation of the user; inhalation monitoring apparatus, configured to, during the inhalation, gather data for determining a measure of the user's lung function and/or lung health; and a processor configured to receive the data from the inhalation monitoring apparatus and, using the data, determine a measure of the user's lung function and/or lung health.

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INHALATION MONITORING SYSTEM AND METHOD

5 CROSS- REFERENCE TO RELATED APPLICATIONS

This non-provisional patent application claims priority to U.S. Provisional Patent Application No. 62/087,567, filed December 4, 2014, U.S. Provisional Patent Application No. 62/087,571, filed December 4, 2014, and U.S. Patent Application No. 14/802,675, 10 filed July 17, 2015, each of which is incorporated by reference herein in its entirety and for all purposes.

FIELD OF THE INVENTION

15 This invention is related to an inhaler, an inhalation monitoring system, and a method for monitoring an inhaler.

BACKGROUND

20 Inhalers or puffers are used for delivering medication into the body via the lungs. They can be used, for example, in the treatment of asthma and chronic obstructive pulmonary disease (COPD). Types of inhalers include metered dose inhalers (MDIs), Soft Mist Inhalers (SMIs), nebulisers and dry powder inhalers (DPIs).

A tidal inhaler is a class of inhaler in which the medication is consumed in multiple 25 successive inhalations (*e.g.*, which may be referred to as tidal breaths) rather than a single inhalation. The patient uses their normal at rest breathing pattern without an exaggerated inhalation flow rate, also known as forced inhalation maneuver.

A spirometer is an apparatus for measuring the volume of air inspired and expired by a 30 patient's lungs. Spirometers measure ventilation, the movement of air into and out of the lungs. From the traces, known as spirograms, output by spirometers, it is possible

to identify abnormal (obstructive or restrictive) ventilation patterns. Existing spirometers use a variety of different measurement methods including pressure transducers, ultrasonic and water gauge.

- 5 Peak flow meters are used to measure peak expiratory flow (PEF), also called peak expiratory flow rate (PEFR). This is a person's maximum speed of expiration. PEF correlates with the airflow through the bronchi and thus the degree of obstruction in the airways. Peak flow readings are lower when the airways are constricted, for example due to an exacerbation of a lung condition. From changes in recorded values, patients and doctors may determine lung functionality, severity of symptoms, and treatment.
10 Peak flow meters can also be used for diagnosis.

Spirometers and peak flow meters are generally used to monitor the lung function and/or lung health of individuals, in particular lung patients suffering from conditions such as asthma and COPD. Lung function is defined according to expiratory measures, such as PEF.
15

Another measure of lung function is forced expiratory volume in 1 second (FEV₁). FEV₁ is the volume of air that can forcibly be blown out in one second, after full inspiration.
20 In obstructive diseases (e.g. asthma, COPD, chronic bronchitis, emphysema) FEV₁ is diminished because of increased airway resistance to expiratory flow.

Patient lung function is generally monitored during appointments with medical practitioners, periodically or in response to a recurrence or worsening of symptoms. For reasons of practicality, monitoring is typically quite infrequent during periods of apparent good health. Reactive treatment is therefore not always administered as soon as it ideally would be, and preventative treatment can be used more than necessary.
25

Some patients find spirometers and peak flow meters tricky to use and may need training and supervision in their use. Due to this, and for reasons of cost, most patients do not possess personal spirometers or peak flow meters.
30

What is needed is an improved means of monitoring lung function and/or health for patients with obstructive lung conditions.

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SUMMARY

According to a first aspect, there is provided an inhalation monitoring system comprising: an inhaler comprising medicament delivery apparatus configured to deliver medicament to a user during an inhalation of the user; inhalation monitoring apparatus configured to, during said inhalation, gather data for determining a measure of the user's lung function and/or lung health; and a processor configured to receive said data from said inhalation monitoring apparatus and, using the data, determine a measure of the user's lung function and/or lung health.

The inhaler could be a dry powder inhaler. The inhaler could be a pressurised metred dose inhaler (pMDI). The inhaler could be a wet nebuliser. The inhaler could be a tidal inhaler.

Said processor could be configured to determine said measure of the user's lung function and/or lung health by determining, from the data, peak inspiratory flow (PIF). Said processor could be configured to determine said measure of the user's lung function and/or lung health by determining, from the data, total inhaled volume.

The inhalation monitoring system could further comprise a user interface. Such a user interface could be configured to provide an indication of said measure of the user's lung function and/or lung health to the user. Such a user interface could be configured to provide an indication of said measure of the user's lung function and/or lung health to a caregiver. Such a user interface could be configured to provide an indication of said measure of the user's lung function and/or lung health to a medical professional.

Said indication could comprise an absolute value. Said indication could comprise a relative value. Said indication could comprise a binary health indicator. Said indication

could comprise a tertiary indicator of whether the measure is above, below, or within a safe zone.

Said indication could be dependent upon data relating to the user.

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The inhalation monitoring system could further comprise a transmitter. Said transmitter could be wireless.

Said transmitter could be configured to send the data to a user device for processing.

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Said transmitter could be configured to send the data to a user device for storage. Said transmitter could be configured to send the data to a user device for provision to the user. Said transmitter could be configured to send the data to a user device for provision to a caregiver. Said transmitter could be configured to send the data to a user device for provision to a medical professional.

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Said transmitter could be configured to send the data to a server for processing. Said transmitter could be configured to send the data to a server for storage. Said transmitter could be configured to send the data to a server for provision to the user. Said transmitter could be configured to send the data to a server for provision to a caregiver.

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Said transmitter could be configured to send the data to a server for provision to a medical professional.

Said transmitter could be configured to send the data to a data cloud for storage.

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Said transmitter could be configured to send said measure to a user device for processing. Said transmitter could be configured to send said measure to a user device for storage. Said transmitter could be configured to send said measure to a user device for provision to the user. Said transmitter could be configured to send said measure to a user device for provision to a caregiver. Said transmitter could be configured to send

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said measure to a user device for provision to a medical professional.

Said transmitter could be configured to send said measure to a server for processing. Said transmitter could be configured to send said measure to a server for storage. Said transmitter could be configured to send said measure to a server for provision to the user. Said transmitter could be configured to send said measure to a server for provision
5 to a caregiver. Said transmitter could be configured to send said measure to a server for provision to a medical professional.

Said transmitter could be configured to send said measure to a data cloud for storage.

10 U.S. Provisional Patent App. Nos. 62/011,808 and 62/135,798, and U.S. Patent Application No. 14/802,675, which are each incorporated by reference herein in their entirety, describe an interface device that supports communications between a medical device and an electronic device. Such an interface could be utilized in the inhalation monitoring system that is described herein.

15 Said processor could be comprised in said inhaler. Said inhalation monitoring apparatus could be comprised in said inhaler. Said inhalation monitoring apparatus could be configured to be connected to said inhaler such that it is in pneumatic communication with a flow channel thereof. Said user interface could be comprised in said inhaler. Said
20 transmitter could be comprised in said inhaler.

Said inhalation monitoring apparatus could comprise a pressure sensor. Said pressure sensor could be a microelectromechanical system (MEMS) pressure sensor. Said pressure sensor could be a barometric MEMS pressure sensor. Said pressure sensor
25 could be a nanoelectromechanical system (NEMS) pressure sensor.

Said inhalation monitoring apparatus could be configured to gather the data by sampling a pressure differential or absolute pressure at a series of time points.

30 Said sampling could be periodic. Said sampling period could be approximately 50ms. The sampling frequency could be 100 Hz, for example.

Said medicament delivery apparatus could be further configured to deliver medicament to the user during a further inhalation of the user subsequent to said inhalation. The further inhalation may be a new breath by the user using a tidal inhaler, or a continuation of the first inhalation by the user using a dry-powder inhaler, for example.

5

Said inhalation monitoring apparatus could be further configured to, during said further inhalation, gather further data for determining a further measure of the user's lung function and/or lung health. Said processor could be further configured to receive said further data from the inhalation monitoring apparatus. Said processor could be further configured to, using the further data, determine a further measure of the user's lung function and/or lung health. Said processor could be further configured to make a comparison of the data with the further data. Said processor could be further configured to make a comparison of the measure of the user's lung function and/or lung health with said further measure of the user's lung function and/or lung health.

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The processor could be further configured to determine efficacy of usage of said inhaler using said comparison.

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The processor could be further configured to predict future changes to the user's lung function and/or lung health using said comparison.

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Said future changes to the user's lung function and/or lung health could comprise exacerbations of an existing respiratory condition such as asthma or chronic obstructive pulmonary disease (COPD).

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The inhalation monitoring system could be configured to provide an alert to the user in response to said processor predicting one of a predetermined set of future changes to the user's lung function and/or lung health. The inhalation monitoring system could be configured to provide an alert to a caregiver in response to said processor predicting one of a predetermined set of future changes to the user's lung function and/or lung health. The inhalation monitoring system could be configured to provide an alert to a

medical professional in response to said processor predicting one of a predetermined set of future changes to the user's lung function and/or lung health.

Said prediction could use data collected from subjects other than the user.

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Said processor could be configured to determine said measure of the user's lung function and/or lung health using a mathematical model such as a regression model.

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Said mathematical model could be of the correlation between total inhaled volume and forced expiratory volume in 1 second (FEV₁). Said mathematical model could be of the correlation between peak inspiratory flow (PIF) and forced expiratory volume in 1 second (FEV₁). Said mathematical model could be of the correlation between total inhaled volume and peak expiratory flow (PEF). Said mathematical model could be of the correlation between peak inspiratory flow (PIF) and peak expiratory flow (PEF).

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For a multiple inhalation tidal inhaler or nebulizer, said mathematical model could be of the correlation between forced expiratory volume in 1 second (FEV₁) and the rate of change of the expiratory flow.

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For a single inhalation dry-powder inhaler, a measurement of the user's lung function and/or lung health may be based upon a single breath by a user. For a tidal inhaler or nebulizer, the measurement may be based upon multiple breaths by the user. It is envisioned that outlying data points generated by the multiple breaths may be rejected, leaving only the good data points available for data processing.

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The mathematical model could take into account biometric data for the user.

Said biometric data could comprise gender. Said biometric data could comprise age. Said biometric data could comprise height. Said biometric data could comprise weight.

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The inhalation monitoring system could further comprise a user interface device operable to switch on and/or off said medicament delivery apparatus such that, when

the medicament delivery apparatus is switched off, said inhaler is usable as a spirometer.

5 Said user interface device could comprise a mouthpiece cover of the inhaler. Said mouthpiece cover could be coupled to the medicament delivery apparatus such that a dose of medicament is made available for inhalation through a mouthpiece of the inhaler each time said cover is opened. The medicament delivery apparatus could be configured such that no further doses of medicament can be made available for inhalation through said mouthpiece until the cover has been completely closed and opened again.

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The inhalation monitoring system could further comprise a placebo inhaler device. Said placebo inhaler device could comprise said inhalation monitoring apparatus. Said placebo inhaler device could be configured to be operably connected to said inhalation monitoring apparatus. Said placebo inhaler device could present substantially the same inhalation flow resistance to a user as said inhaler.

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The inhalation monitoring system could comprise a battery configured to power the medicament delivery apparatus. The inhalation monitoring system could comprise a battery configured to power the inhalation monitoring apparatus. The inhalation monitoring system could comprise a battery configured to power the processor.

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The inhalation monitoring system could further comprise memory configured to store the data. The inhalation monitoring system could further comprise memory configured to store said measure.

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The medicament delivery apparatus of the inhalation monitoring system may comprise a medicament, and/or may be part of a kit that comprises the inhalation monitoring system and a medicament. The medicament may comprise one or more active ingredients, for example, one or more of a long-acting muscarinic antagonist (LAMA), a short-acting muscarinic antagonist (SAMA), a long-acting β_2 -agonist (LABA), a short-acting β_2 -agonist (SABA), and/or an inhaled corticosteroid (ICS).

30

According to a second aspect there is provided a method comprising: using an inhaler, delivering medicament to a user during an inhalation of the user; during said inhalation, gathering data for determining a measure of the user's lung function and/or lung health; and using the data, making a determination of a measure of the user's lung function
5 and/or lung health.

The inhaler could be a dry powder inhaler. The inhaler could be a pressurised metered dose inhaler (pMDI). The inhaler could be a wet nebuliser. The inhaler could be a tidal inhaler.
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Said determination could be made by determining, from the data, peak inspiratory flow (PIF). Said determination could be made by determining, from the data, total inhaled volume.

The method could further comprise providing an indication of said measure of the user's lung function and/or lung health to the user by means of a user interface. The method could further comprise providing an indication of said measure of the user's lung function and/or lung health to a caregiver by means of a user interface. The method could further comprise providing an indication of said measure of the user's lung function and/or lung
15 health to a medical professional by means of a user interface.
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Said indication could comprise an absolute value. Said indication could comprise a relative value. Said indication could comprise a binary health indicator. Said indication could comprise a tertiary indicator of whether the measure is above, below, or within a safe zone.
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Said indication could be dependent upon data relating to the user.

The method could further comprise, by means of a transmitter, sending the data to a user device for processing. The method could further comprise, by means of a transmitter, sending the data to a user device for storage. The method could further comprise, by means of a transmitter, sending the data to a user device for provision to
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the user. The method could further comprise, by means of a transmitter, sending the data to a user device for provision to a caregiver. The method could further comprise, by means of a transmitter, sending the data to a user device for provision to a medical professional.

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The method could further comprise, by means of a transmitter, sending the data to a server for processing. The method could further comprise, by means of a transmitter, sending the data to a server for storage. The method could further comprise, by means of a transmitter, sending the data to a server for provision to the user. The method could further comprise, by means of a transmitter, sending the data to a server for provision to a caregiver. The method could further comprise, by means of a transmitter, sending the data to a server for provision to a medical professional.

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The method could further comprise, by means of a transmitter, sending the data to a data cloud for storage.

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The method could further comprise, by means of a transmitter, sending said measure to a user device for processing. The method could further comprise, by means of a transmitter, sending said measure to a user device for storage. The method could further comprise, by means of a transmitter, sending said measure to a user device for provision to the user. The method could further comprise, by means of a transmitter, sending said measure to a user device for provision to a caregiver. The method could further comprise, by means of a transmitter, sending said measure to a user device for provision to a medical professional.

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The method could further comprise, by means of a transmitter, sending said measure to a server for processing. The method could further comprise, by means of a transmitter, sending said measure to a server for storage. The method could further comprise, by means of a transmitter, sending said measure to a server for provision to the user. The method could further comprise, by means of a transmitter, sending said measure to a server for provision to a caregiver. The method could further comprise,

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by means of a transmitter, sending said measure to a server for provision to a medical professional.

The method could further comprise, by means of a transmitter, sending said measure
5 to a data cloud for storage.

Said transmitter could be a wireless transmitter.

As noted above, according to the second aspect of the invention, there is provided a
10 method comprising: using an inhaler, delivering medicament to a user during an inhalation of the user; during said inhalation, gathering data for determining a measure of the user's lung function and/or lung health; and using the data, making a determination of a measure of the user's lung function and/or lung health.

15 Said gathering could be done by said inhaler. Said determination could be made by said inhaler.

Said gathering could be done by inhalation monitoring apparatus. Said method could
20 further comprise connecting said inhalation monitoring apparatus to the inhaler such that the inhalation monitoring apparatus is in pneumatic communication with a flow channel of the inhaler.

Said user interface could be comprised in said inhaler. Said transmitter could be comprised in said inhaler.

25 Said gathering could be performed by means of a pressure sensor. Said pressure sensor could be a microelectromechanical system (MEMS) pressure sensor. Said pressure sensor could be a barometric MEMS pressure sensor. Said pressure sensor could be a nanoelectromechanical system (NEMS) pressure sensor.

30 Said data gathering could comprise sampling a pressure differential at a series of time points. Said data gathering could also comprise sampling an absolute pressure at a series of time points.

Said sampling could be periodic.

5 Said sampling period could be approximately 50ms. The sampling frequency could be 100 Hz, for example.

10 The method could further comprise delivering medicament to the user during a further inhalation of the user subsequent to said inhalation. The method could further comprise during said further inhalation, gathering further data for determining a further measure of the user's lung function and/or lung health. The method could further comprise using the further data, making a determination of a further measure of the user's lung function and/or lung health. The method could further comprise making a comparison of the data with the further data. The method could further comprise making a comparison of the measure of the user's lung function and/or lung health with said further measure of the user's lung function and/or lung health.

15 The method could further comprise determining efficacy of usage of said inhaler using said comparison.

20 The method could further comprise predicting future changes to the user's lung function and/or lung health using said comparison.

25 Said future changes to the user's lung function and/or lung health could comprise exacerbations of an existing respiratory condition such as asthma, chronic obstructive pulmonary disease (COPD), respiratory syncytial virus (RSV), Cystic Fibrosis (CF), idiopathic pulmonary fibrosis (IPF), or pulmonary embolism (PE).

30 The method could further comprise providing an alert to the user in response to said predicting. The method could further comprise providing an alert to a caregiver in response to said predicting. The method could further comprise providing an alert to a medical professional in response to said predicting.

Said prediction could use data collected from subjects other than the user.

Said determination of said measure of the user's lung function and/or lung health could use a mathematical model. Said mathematical model could be a regression model.

5

Said mathematical model could be of the correlation between total inhaled volume and forced expiratory volume in 1 second (FEV₁). Said mathematical model could be of the correlation between peak inspiratory flow (PIF) and forced expiratory volume in 1 second (FEV₁). Said mathematical model could be of the correlation between total inhaled volume and peak expiratory flow (PEF). Said mathematical model could be of the correlation between peak inspiratory flow (PIF) and peak expiratory flow (PEF).

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The mathematical model could take into account biometric data for the user.

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Said biometric data could comprise gender. Said biometric data could comprise age. Said biometric data could comprise height. Said biometric data could comprise weight.

The method could further comprise: switching off a medicament delivery function of the inhaler; and using the inhaler as a spirometer.

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For a single inhalation dry-powder inhaler, for example, switching off said medicament delivery function could comprise opening a mouthpiece cover of the inhaler. Said cover could be configured such that a dose of medicament is made available for inhalation through a mouthpiece of the inhaler each time the cover is opened. The inhaler could be configured such that no further doses of medicament can be made available for inhalation through the mouthpiece until the cover has been completely closed and opened again.

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The method could further comprise using a placebo inhaler device.

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Said gathering could be performed by inhalation monitoring apparatus. Said placebo inhaler device could comprise said inhalation monitoring apparatus. Said placebo inhaler

device could be configured to be operably connected to said inhalation monitoring apparatus.

5 Said placebo inhaler device could present substantially the same inhalation flow resistance to a user as said inhaler. For a multiple inhalation tidal inhaler or a wet nebulizer, which may have a lower inhalation flow resistance than a dry-powder inhaler, it may be advantageous to use a special non-drug cartridge having a defined inhalation flow resistance. The non-drug cartridge could electronically identify itself to the inhaler by the same means that is used to identify the drug within a cartridge, e.g., via an electrically erasable programmable read-only memory.

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The method could further comprise storing the data and/or said measure in memory.

BRIEF DESCRIPTION OF THE DRAWING FIGURES

Aspects of the present invention will now be described by way of example with reference to the accompanying figures. In the figures:

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Figure 1a illustrates an example correlation between PEF and the maximum flow measured during inhalation;

Figure 1b illustrates an example correlation between FEV1 and total inhaled volume;

Figure 2 schematically illustrates an example inhalation monitoring system; and

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Figure 3 is a flowchart of an example inhalation monitoring method.

DETAILED DESCRIPTION

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The following description is presented to enable any person skilled in the art to make and use the system, and is provided in the context of a particular application. Various modifications to the disclosed embodiments will be readily apparent to those skilled in the art.

20

The general principles defined herein may be applied to other embodiments and applications without departing from the spirit and scope of the present invention. Thus, the present invention is not intended to be limited to the embodiments shown, but is to be accorded the widest scope consistent with the principles and features disclosed herein.

25

Many lung patients are prescribed inhalers so that they or a caregiver can administer medicament to them as a routine preventative measure, to ease an exacerbation, or both. Such patients and caregivers are trained in the use of these inhalers and become very familiar with them. It is therefore proposed to monitor patients' lung function using their inhalers. Monitoring lung health while administering medication reduces the time and effort required from patients, caregivers and medical professionals to manage lung conditions.

30

This has not been previously considered since, as explained above, lung function is generally assessed using expiratory measures and dry powder inhalers, for example, are not generally designed to permit exhalation. In some cases, for example some dry powder inhalers, exhalation into inhalers can impair their function (e.g., if moisture from an exhalation causes powdered medicament to form clumps, making even administration more difficult).

However, the applicant has established that there are correlations between some expiratory measures of lung function and some inspiratory measures. For example, see Figure 1a, showing a correlation between PEF and the maximum flow measured during inhalation (peak inspiratory flow, PIF), and Figure 1b, showing a correlation between FEV1 and total inhaled volume. Regression lines and their equations are indicated on the plots, where:

x_1 = gender (male = 0; female = 1)
 x_2 = age/years
 x_3 = height/cm
 x_4 = weight/kg
 x_5 = PEF/l.min⁻¹
 x_6 = FEV1/l.min⁻¹
 y_1 = inhaled volume/l
 y_2 = PIF/l

It is therefore proposed to process inhalation data gathered while administering medicament with an inhaler in order to determine lung function and/or health.

Figure 2 schematically illustrates an example inhalation monitoring system 200. An inhaler 210 comprises medicament delivery apparatus 211. This could for example be as per the dry powder inhalers described in any of PCT patent application publication numbers WO 01/97889, WO 02/00281, WO 2005/034833 or WO 2011/054527, which are incorporated in their entirety herein. Inhalation monitoring systems could also comprise other types of inhalers/nebulisers, for example, pressurised metred dose

inhalers (pMDIs) or wet nebulisers. The inhalers could require forced inspiratory manoeuvres or only tidal breathing.

5 Inhalation monitoring apparatus 220 may also be comprised in the inhaler as shown, or may be comprised in a separate unit connected to it. The inhalation monitoring apparatus could for example comprise a miniature (e.g., microelectromechanical, MEMS, or nanoelectromechanical, NEMS) pressure sensor as described in any of US patent application numbers 62/043,126 to Morrison, 62/043,120 to Morrison, and 62/043,114 to Morrison, which are incorporated in their entirety herein. Other suitable
10 arrangements could be envisaged. For those making use of a pressure sensor, said sensor should be in pneumatic communication with an airflow channel of the inhaler through which the user inhales.

15 A processor 230 communicates with the inhalation monitoring apparatus in order to process data collected by the inhalation monitoring apparatus to determine a measure of the user's lung function and/or health. The processor could be comprised in the inhaler as shown, or if the inhalation monitoring apparatus is comprised in a separate accessory unit, the processor could also be comprised in said accessory unit. If the inhalation monitoring apparatus is equipped with a wired or wireless transmitter 221,
20 the processor could be in a separate device, for example a user device such as a smartphone, tablet, laptop or PC. If the inhalation monitoring apparatus is equipped with a transmitter capable of communicating with a network such as the internet, the processing could be done remotely, for example at a medical professional's PC or on a health service, inhaler manufacturer or cloud server. For example, any of the
25 abovementioned devices or servers could also be used for data storage. Processor 230 may be made up of multiple processors in any of the abovementioned locations, for example some basic processing may be done on board the inhaler, while more detailed analysis is offloaded to a remote device or server.

30 The inhaler may comprise a user interface 240 for providing information relating to use of the inhaler and/or determined lung function and/or lung health. This could, for example, be a screen, indicator light, indicator buzzer, speaker, traditional dose counter

tape, vibrating alert etc. or any combination of these or similar. Alternatively or additionally, such information could be provided via one or more user interfaces of a user device of the patient or a caregiver or medical professional.

- 5 The system could also comprise a memory 250 for storing the collected data, calculation results and computer code instructions for execution by the processor. As with the processor, the memory could be located in the inhaler or an external device or server.

10 The electronic component of the inhaler could be powered by a battery 212 so that the inhaler can be portable.

15 The inhaler could further comprise switching means for putting the medicament delivery apparatus in or out of operation. When the medicament delivery apparatus is not functioning, the inhaler can be used as a spirometer. As one example, electronic switching means could be provided if the medicament delivery apparatus is under
20 electronic (e.g., push-button) control. As another example, PCT patent application publication number WO 2005/034833, which is incorporated by reference herein in its entirety, describes a mechanism for a metered dose dry powder inhaler in which a metering cup measures out a dose of medicament from a hopper and is moved to a dosing position by action of a yoke linked to a mouthpiece cover. Thus, opening the mouthpiece cover primes the inhaler for use and once a dose has been inhaled, further dosing is not possible until the cover has been closed and opened again. Using such an inhaler with the inhalation monitoring apparatus proposed herein, a patient could take
25 their dose of medicament and, before closing the mouthpiece cover, make one or more further inhalations through the mouthpiece for the purposes of further data collection. This allows greater volumes of data to be collected without risking the patient overdosing. As yet another example, a spirometer cartridge could be connected to a replaceable cartridge tidal inhaler, and a patient could make one or more further inhalations through the spirometer cartridge for the purpose of further data collection.

30 Alternatively or additionally, the inhaler described above could be provided in a kit with a placebo or dummy inhaler which has a similar flow resistance to the real inhaler, but

which either does not comprise medicament delivery apparatus, is empty or is loaded with a placebo substance such as lactose. The placebo inhaler could comprise similar inhalation monitoring apparatus to that described above, or could be connectable to such apparatus.

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If inhaler 210 were a wet nebulizer, for example, then all of the electronic components could be located in a module that is removably connected to the inhalation port in order to protect the electronics from exposure to fluid. The module could be configured to be connected to different wet nebulizers of varying shape and size. The module could

10

include a flow channel having a defined inhalation flow resistance that is higher than the inhalation flow resistance of the wet nebulizer alone (e.g., without the module).

Figure 3 is a flowchart of an example inhalation monitoring method 300. At 310, inhalation (through an inhaler) commences. At 320, medicament is delivered via the inhaler. At 330, data concerning said inhalation is collected. At 340, inhalation ends. At

15

350, the data is processed to make a determination of a measure of lung function and/or lung health. The order of steps 320 and 330 could be reversed or they could be carried out partially or fully in parallel. Step 350 could occur before, during or after 340 and before, after, or fully or partially in parallel with 320.

20

The data could also be used for adherence monitoring by a medical practitioner, e.g., to ensure that the inhaler is being used properly by the user.

The processing could comprise use of a mathematical model such as the regression models illustrated in Figure 1.

25

Method 300 could be repeated each time the inhaler is used, which could for example be daily. Data gathered from multiple uses of the inhaler and/or determinations made from the data could be stored and compared to provide an indication of the progression of a condition over time. This information could be used to determine efficacy of the current treatment regime and inform any changes which may be required. The processor

30

may also be capable of using the data and/or determinations to predict future changes in lung function and/or lung health. This prediction could be based on date (e.g., only

on data) collected from the patient in question, and/or could incorporate data collected from other patients too. For example, data from users of many inhalers as described above could be collated and used to identify patterns in inhalation data changes preceding exacerbations of particular lung conditions. The processing logic could thus be self-learning. If a particular patient's data is then seen to match the beginning of such a pattern, they or their caregiver or medical practitioner could be alerted so that any required changes to a treatment regime (for example, increased dosage, additional medications or therapies) can be made to help avoid an exacerbation.

10 The data collected by the inhalation monitoring apparatus could be, for example, a time series of pressure differential measurements or absolute pressure measurements. Measurements could be made periodically, for example every 10ms, 50ms or 100ms over e.g. 2, 5 or 10 seconds. Data collection may be reset between uses of the inhalation monitoring apparatus.

15 The user interface could provide a numerical value, for example of measured PIF, calculated total inhaled volume, calculated PEF, calculated FEV1 or a fraction or percentage of one of these relative to an ideal value for the particular patient (e.g., said ideal value could be chosen based on biometric data such as age, gender, height, weight etc.). Alternatively or additionally, it could provide a binary indicator as to whether or not the measured value is within a healthy range, or a tertiary indicator as to whether the measured value is below, above or within a healthy range. Boundaries of such a healthy range could again depend on biometric data stored for the particular patient. The user interface could alternatively or additionally be used to indicate number of doses taken or number of doses remaining in a disposable inhaler, refillable hopper or disposable cartridge. Another alternative or additional indication could be whether the inhaler has been used correctly, for example so that the patient or a caregiver or medical professional is alerted to missed doses, inhalations that are too short or weak for effective drug administration, or that medication has otherwise been taken incorrectly, and/or receives confirmation that medication has been taken correctly.

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25
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The inhaler is preferably directed to the treatment of respiratory disorders such as asthma and/or COPD. A range of classes of medicaments have been developed to treat respiratory disorders, and each class has differing targets and effects.

5 Bronchodilators are employed to dilate the bronchi and bronchioles, decreasing resistance in the airways, thereby increasing the airflow to the lungs. Bronchodilators may be short-acting or long-acting. Typically, short-acting bronchodilators provide a rapid relief from acute bronchoconstriction, whereas long-acting bronchodilators help control and prevent longer-term symptoms.

10

Different classes of bronchodilators target different receptors in the airways. Two commonly used classes are anticholinergics and β_2 -agonists.

15 Anticholinergics (or "antimuscarinics") block the neurotransmitter acetylcholine by selectively blocking its receptor in nerve cells. On topical application, anticholinergics act predominantly on the M3 muscarinic receptors located in the airways to produce smooth muscle relaxation, thus producing a bronchodilatory effect. Preferred examples of long-acting muscarinic antagonists (LAMAs) include tiotropium (bromide), oxitropium (bromide), aclidinium (bromide), ipratropium (bromide) glycopyrronium (bromide),
20 oxybutynin (hydrochloride or hydrobromide), tolterodine (tartrate), trospium (chloride), solifenacin (succinate), fesoterodine (fumarate) and darifenacin (hydrobromide). In each case, particularly preferred salt/ester forms are indicated in parentheses. Preferred examples of short-acting muscarinic antagonists (SAMAs) include tropicamide and cyclopentolate.

25

β_2 -Adrenergic agonists (or " β_2 -agonists") act upon the β_2 -adrenoceptors which induces smooth muscle relaxation, resulting in dilation of the bronchial passages. Preferred long-acting β_2 -agonists (LABAs) include formoterol (fumarate), salmeterol (xinafoate), indacaterol (maleate), bambuterol (hydrochloride), clenbuterol (hydrochloride),
30 olodaterol (hydrochloride), carmoterol (hydrochloride), tulobuterol (hydrochloride) and vilanterol (triphenylacetate). Examples of short-acting β_2 -agonists (SABAs) include salbutamol (sulfate), terbutaline (sulfate), pirbuterol (acetate), metaproterenol

(sulfate), and albuterol. In each case, particularly preferred salt/ester forms are indicated in parentheses.

5 Another class of medicaments employed in the treatment of respiratory disorders are inhaled corticosteroids (ICSs). ICS are steroid hormones used in the long-term control of respiratory disorders. They function by reducing the airway inflammation. Preferred examples include budesonide, beclomethasone (dipropionate), fluticasone (propionate or furoate), mometasone (furoate), ciclesonide and dexamethasone (sodium). In each case, particularly preferred salt/ester forms are indicated in parentheses.

10

The active ingredients may be administered in combination, and both combination therapies and combination products have been proposed. Examples of combination treatments and products disclosed in the art are set out in WO 2004/019985, WO 15 2007/071313, WO 2008/102128 and WO 2011/069197. The active ingredients can be a combination of a LAMA, LABA and an ICS. They may be a double combination of a LAMA and a LABA, a LAMA and an ICS, a LABA and an ICS, and/or the like. They may also be a combination of a LAMA, a LABA, and an ICS.

Example combinations are:

- 20 oxybutynin (hydrochloride or hydrobromide) and formoterol (fumarate)
darifenacin (hydrobromide) and formoterol (fumarate)
oxybutynin (hydrochloride or hydrobromide), formoterol (fumarate) and beclomethasone (dipropionate)
darifenacin (hydrobromide), formoterol (fumarate) and beclomethasone (dipropionate)
25 oxybutynin (hydrochloride or hydrobromide) and salmeterol (xinafoate)
darifenacin (hydrobromide) and salmeterol (xinafoate)
oxybutynin (hydrochloride or hydrobromide), salmeterol (xinafoate) and fluticasone (propionate)
darifenacin (hydrobromide), salmeterol (xinafoate) and fluticasone (propionate)
30 glycopyrronium (bromide) and indacaterol (maleate)
glycopyrronium (bromide) and formoterol (fumarate)
tiotropium (bromide) and formoterol (fumarate)

tiotropium (bromide) and carmoterol (hydrochloride)
tiotropium (bromide) and olodaterol (hydrochloride)
tiotropium (bromide) and indacaterol (maleate)
budesonide and formoterol (fumarate)

5

A number of approaches have been taken in formulating these classes of active ingredients for delivery by inhalation, such as via a dry powder inhaler (DPI), a pressurised metered dose inhaler (pMDI), or a nebuliser.

10 The API of the medicament should penetrate deep into the lung in order to reach their site of action. Therefore, the APIs are micronized to obtain particles having the required size, typically a mass medium aerodynamic diameter (MMAD) of 1-5 μm .

15 The medicament may be delivered as pure drug, but more appropriately, it is preferred that medicaments are delivered together with excipients (carriers) which are suitable for inhalation. Suitable excipients include organic excipients such as polysaccharides (e.g. starch, cellulose and the like), lactose, glucose, mannitol, amino acids, and maltodextrins, and inorganic excipients such as calcium carbonate or sodium chloride. Lactose is a preferred excipient.

20

Particles of powdered medicament and/or excipient may be produced by conventional techniques, for example by micronisation, milling or sieving.

25 Additionally, medicament and/or excipient powders may be engineered with particular densities, size ranges, or characteristics. Particles may comprise active agents, surfactants, wall forming materials, or other components considered desirable by those of ordinary skill.

30 The medicament may be incorporated into the reservoir of an inhaler or into a canister to be placed inside of an inhaler. Alternatively, the medicament may be presented separately to the inhaler, for example in a blister strip of unit doses or capsules which can form a kit of parts with the inhaler.

The applicant hereby discloses in isolation each individual feature described herein and any combination of two or more such features, to the extent that such features or combinations are capable of being carried out based on the present specification as a whole in the light of the common general knowledge of a person skilled in the art, irrespective of whether such features or combinations of features solve any problems disclosed herein, and without limitation to the scope of the claims. The applicant indicates that aspects of the present invention may consist of any such individual feature or combination of features. In view of the foregoing description it will be evident to a person skilled in the art that various modifications may be made within the scope of the invention.

What is claimed is:

1. An inhalation monitoring system comprising:
an inhaler comprising a medicament delivery apparatus configured to deliver
5 medicament to a user during an inhalation of the user;
an inhalation monitoring apparatus configured to, during said inhalation, gather
data for determining a measure of the user's lung function and/or lung health; and
a processor configured to receive said data from said inhalation monitoring
apparatus and, using the data, determine a measure of the user's lung function and/or
10 lung health.
2. The inhalation monitoring system of claim 1, wherein the inhaler is a dry powder
inhaler.
- 15 3. The inhalation monitoring system of claim 1, further comprising a user interface
configured to provide an indication of said measure of the user's lung function and/or
lung health to at least one of the user, a caregiver, or a medical professional.
4. The inhalation monitoring system of claim 1, further comprising a transmitter.
20
5. The inhalation monitoring system of claim 4, wherein said transmitter is
configured to send the data and/or said measure to one or more of:
a user device and/or server for one or more of processing, storing, or
provisioning to one or more of the user, a caregiver, or a medical professional; and
25 a data cloud for storage.
6. The inhalation monitoring system of claim 1, wherein said processor is comprised
in said inhaler.
- 30 7. The inhalation monitoring system of claim 1, wherein said inhalation monitoring
apparatus is comprised in said inhaler.

8. The inhalation monitoring system of claim 1, wherein said inhalation monitoring apparatus comprises a pressure sensor.

9. The inhalation monitoring system of claim 1, further comprising a user interface device operable to switch on and/or off said medicament delivery apparatus such that, when the medicament delivery apparatus is switched off, said inhaler is usable as a spirometer.

10. The inhalation monitoring system of claim 9, wherein said user interface device comprises a mouthpiece cover of the inhaler coupled to the medicament delivery apparatus such that a dose of medicament is made available for inhalation through a mouthpiece of the inhaler each time said cover is opened, the medicament delivery apparatus being configured such that no further doses of medicament can be made available for inhalation through said mouthpiece until the cover has been completely closed and opened again.

11. The inhalation monitoring system of claim 1, wherein the medicament delivery apparatus comprises a medicament.

12. A kit comprising the inhalation monitoring system of claim 1 and a medicament.

13. The inhalation monitoring system of claim 11 or the kit of claim 12, wherein the medicament comprises one or more active ingredients selected from a long-acting muscarinic antagonist (LAMA), a short-acting muscarinic antagonist (SAMA), a long-acting β_2 -agonist (LABA), a short-acting β_2 -agonist (SABA), and an inhaled corticosteroid (ICS).

14. A method comprising:
using an inhaler, delivering medicament to a user during an inhalation of the user;
during said inhalation, gathering data for determining a measure of the user's lung function and/or lung health; and

determining a measure of the user's lung function and/or lung health using the gathered data.

15. The method of claim 14, wherein said determination is made by determining
5 peak inspiratory flow (PIF) and/or total inhaled volume from the data.

16. The method of either of claim 14, further comprising:
delivering medicament to the user during a further inhalation of the user
subsequent to said inhalation;

10 during said further inhalation, gathering further data for determining a further
measure of the user's lung function and/or lung health;

using the further data, determining a further measure of the user's lung function
and/or lung health; and

15 making a comparison of the data with the further data and/or a comparison of
the measure of the user's lung function and/or lung health with said further measure of
the user's lung function and/or lung health.

17. The method of claim 16, further comprising determining efficacy of usage of said
20 inhaler using said comparison.

18. The method of claim 16, further comprising predicting future changes to the
user's lung function and/or lung health using said comparison.

19. The method of claim 18, wherein said future changes to the user's lung function
25 and/or lung health comprise exacerbations of an existing respiratory condition such as
asthma or chronic obstructive pulmonary disease (COPD).

20. The method of claim 19, further comprising providing an alert to one or more of
the user, a caregiver, or a medical professional in response to said predicting.

30 21. The method of claim 14, wherein said determination of said measure of the user's
lung function and/or lung health uses a mathematical model.

22. The method of claim 21, wherein said mathematical model is of the correlation between either total inhaled volume or peak inspiratory flow (PIF) and either forced expiratory volume in 1 second (FEV₁) or peak expiratory flow (PEF).

5

23. The method of claim 22, wherein the mathematical model takes into account biometric data for the user.

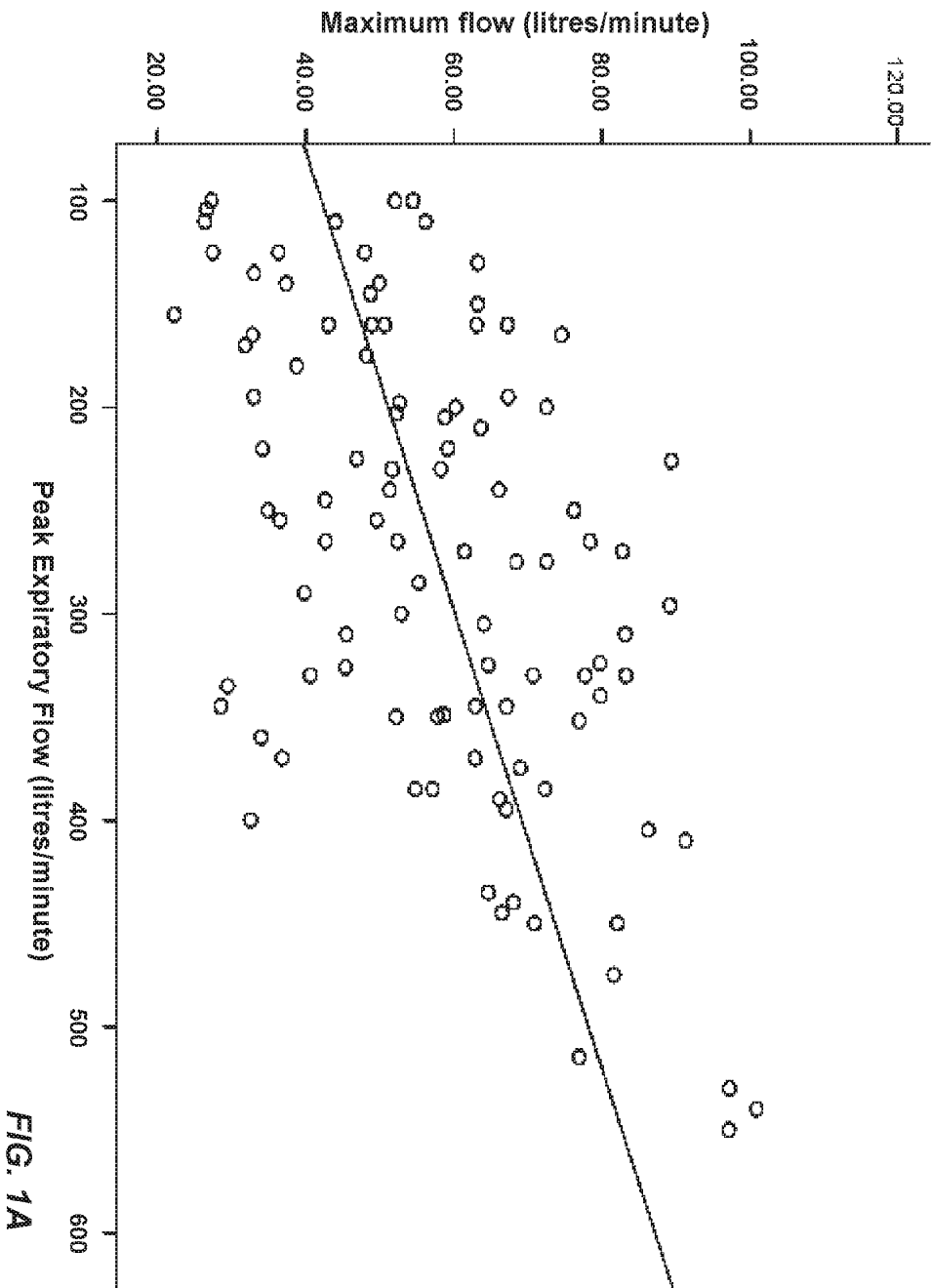


FIG. 1A

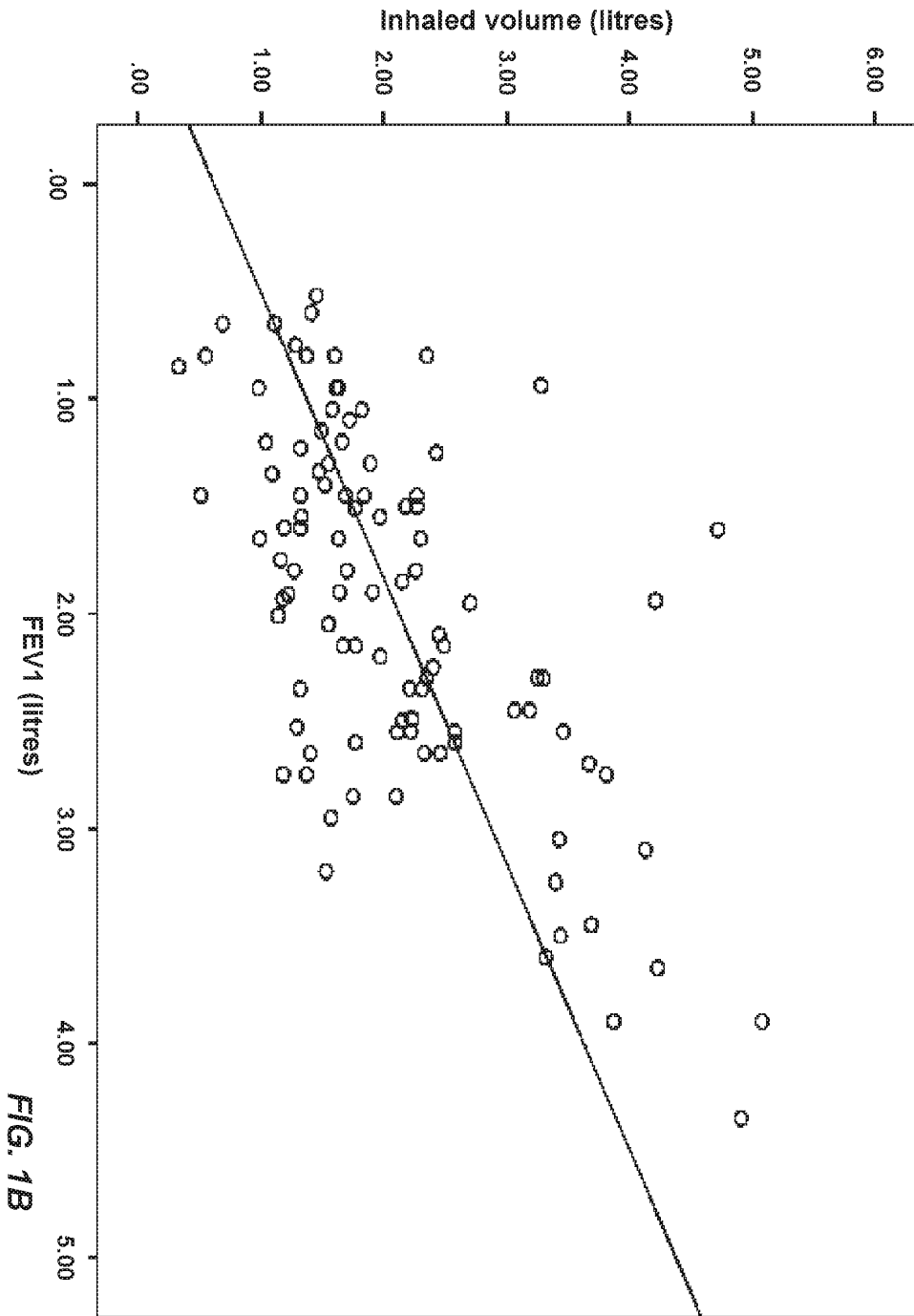


FIG. 1B

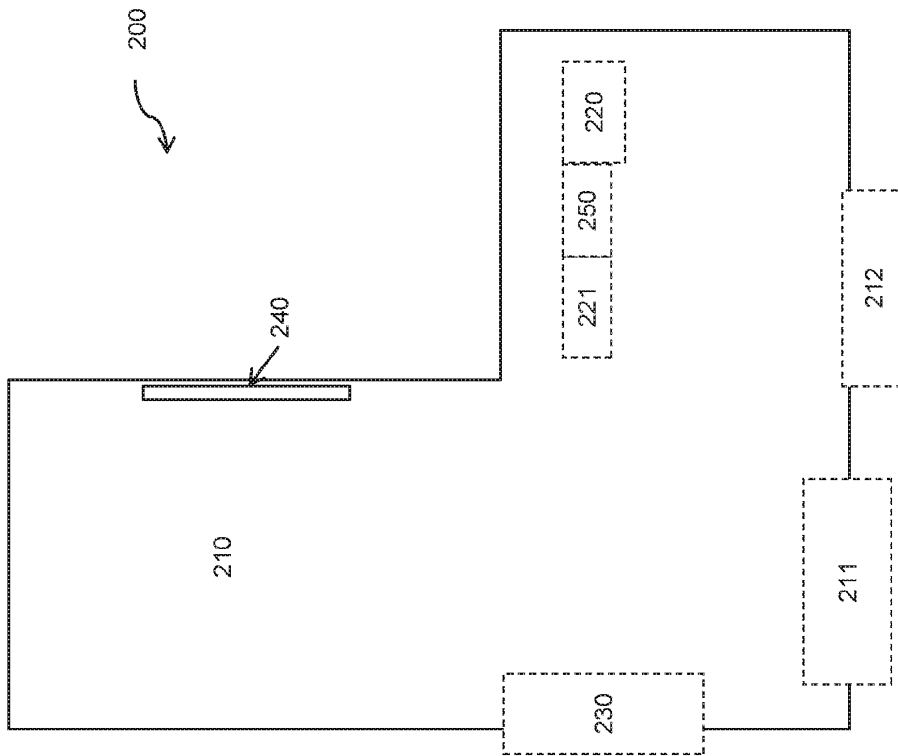


FIG. 2

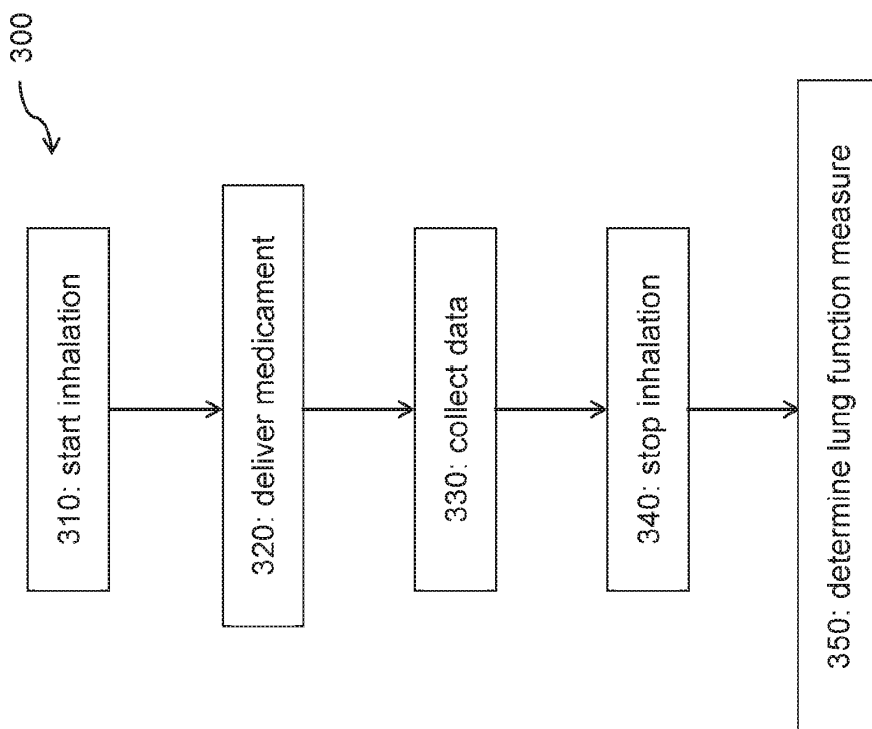


FIG. 3

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2015/064017

A. CLASSIFICATION OF SUBJECT MATTER INV. A61M15/00 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) A61M A61B		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/046426 A2 (SPIROJET MEDICAL LTD [IL]; KRASILCHIKOV YEHEZKEL [IL]; LITVAK ANNA [IL] 26 May 2005 (2005-05-26) the whole document -----	1-13
X	US 2009/156952 A1 (HUNTER C ERIC [US] ET AL) 18 June 2009 (2009-06-18) The whole document, especially paragraph [0034] -----	1-13
X	WO 2008/149959 A1 (CANON KK [JP]; SAKURADA NAOKO [JP]; SUGITA MASARU [JP]; KANEKO HIDEKI) 11 December 2008 (2008-12-11) page 28, line 9 - page 32, line 15 ----- -/--	1-13
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
* Special categories of cited documents :		
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	
"P" document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search	Date of mailing of the international search report	
16 February 2016	29/02/2016	
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Borowski, Aleksander	

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INTERNATIONAL SEARCH REPORT

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2013/098714 A1 (KONINKL PHILIPS ELECTRONICS NV [NL]) 4 July 2013 (2013-07-04) The whole document, especially paragraphs [15]-[17] -----	1-13
X	US 2014/202457 A1 (ADDINGTON W ROBERT [US] ET AL) 24 July 2014 (2014-07-24) The whole document, especially paragraph [0119] -----	1-13

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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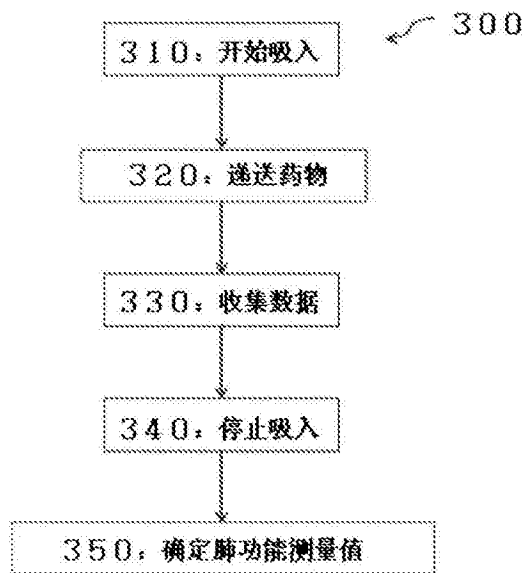
权利要求书2页 说明书12页 附图3页

(54)发明名称

吸入监测系统和方法

(57)摘要

吸入监测系统包括吸入器,该吸入器具有经配置在使用者的吸入期间向使用者递送药物的药物递送仪器;吸入监测仪器,该吸入监测仪器经配置在该吸入期间采集数据用于确定使用者的肺功能和/或肺健康的测量值;以及处理器,该处理器经配置接收来自该吸入监测仪器的数据并且使用该数据确定使用者的肺功能和/或肺健康的测量值。



1. 吸入监测系统,所述吸入监测系统包括:
吸入器,所述吸入器包括经配置在使用者的吸入期间向使用者递送药物的药物递送仪器;
吸入监测仪器,所述吸入监测仪器经配置在所述吸入期间采集数据用于确定使用者的肺功能和/或肺健康的测量值;以及
处理器,所述处理器经配置接收来自所述吸入监测仪器的所述数据并且,使用所述数据确定使用者的肺功能和/或肺健康的测量值。
2. 根据权利要求1所述的吸入监测系统,其中所述吸入器是干粉吸入器。
3. 根据权利要求1所述的吸入监测系统,所述吸入监测系统进一步包括用户界面,所述用户界面经配置向使用者、照料者或医学专家中的至少一者提供所述使用者的肺功能和/或肺健康的测量值的指示。
4. 根据权利要求1所述的吸入监测系统,所述吸入监测系统进一步包括发射器。
5. 根据权利要求4所述的吸入监测系统,其中所述发射器经配置向下列中的一者或多者发送数据和/或所述测量值:
用于处理、存储或向使用者、照料者或医学专家中的一者或多者提供中的一者或多者的用户装置和/或服务器;以及
用于存储的数据云。
6. 根据权利要求1所述的吸入监测系统,其中所述处理器被包括在所述吸入器中。
7. 根据权利要求1所述的吸入监测系统,其中所述吸入监测仪器被包括在所述吸入器中。
8. 根据权利要求1所述的吸入监测系统,其中所述吸入监测仪器包括压力传感器。
9. 根据权利要求1所述的吸入监测系统,所述吸入监测系统进一步包括用户界面装置,所述用户界面装置能够打开和/或关闭所述药物递送仪器使得当所述药物递送仪器被关闭时,所述吸入器可用作呼吸量计。
10. 根据权利要求9所述的吸入监测系统,其中所述用户界面装置包括连接到所述药物递送仪器的吸入器的吸口盖子,使得每当打开所述盖子时,一剂药物是可用于通过吸入器的吸口吸入,所述药物递送仪器经配置使得没有进一步剂量的药物可用于通过所述吸口吸入直到所述盖子已经再次完全地被关闭和打开。
11. 根据权利要求1所述的吸入监测系统,其中所述药物递送仪器包括药物。
12. 包括权利要求1所述的吸入监测系统和药物的成套工具。
13. 根据权利要求11所述的吸入监测系统或权利要求12所述的成套工具,其中所述药物包括选自下列中的一种或多种活性成分:
长效毒蕈碱拮抗剂(LAMA)、短效毒蕈碱拮抗剂(SAMA)、长效 β_2 -激动剂(LABA)、短效 β_2 -激动剂(SABA)和吸入皮质激素(ICS)。
14. 一种方法,所述方法包括:
使用吸入器,在使用者的吸入期间,向使用者递送药物;
在所述吸入期间,采集数据用于确定使用者的肺功能和/或肺健康的测量值;以及
使用采集的数据确定使用者的肺功能和/或肺健康的测量值。
15. 根据权利要求14所述的方法,其中所述确定是通过从数据确定最大吸气流量(PIF)

和/或总的吸入量做出的。

16. 根据权利要求14所述的方法,所述方法进一步包括:

在继所述吸入之后使用者的进一步吸入期间向使用者递送药物;

在所述进一步吸入期间,采集进一步数据用于确定使用者的肺功能和/或肺健康的进一步测量值;

使用所述进一步数据,确定使用者的肺功能和/或肺健康的进一步测量值;以及

比较所述数据和所述进一步数据和/或比较使用者的肺功能和/或肺健康的测量值和所述使用者的肺功能和/或肺健康的进一步测量值。

17. 根据权利要求16所述的方法,所述方法进一步包括通过使用所述比较确定使用所述吸入器的功效。

18. 根据权利要求16所述的方法,所述方法进一步包括通过使用所述比较预测使用者的肺功能和/或肺健康的未来变化。

19. 根据权利要求18所述的方法,其中所述使用者的肺功能和/或肺健康的未来变化包括目前的呼吸状况比如哮喘或慢性阻塞性肺病(COPD)的恶化。

20. 根据权利要求19所述的方法,所述方法进一步包括在响应所述预测中向使用者、照料者或医学专家中的一者或多者提供警报。

21. 根据权利要求14所述的方法,其中所述使用者的肺功能和/或肺健康的测量值的所述确定使用数学模型。

22. 根据权利要求21所述的方法,其中所述数学模型属于总的吸入量或最大吸入流量(PIF)和1秒内的用力呼气量(FEV₁)或最大呼气流量(PEF)之间的关联性。

23. 根据权利要求22所述的方法,其中所述数学模型考虑使用者的生物特征数据。

吸入监测系统和方法

[0001] 相关申请的交叉参考

[0002] 该非临时专利申请要求美国临时专利申请号62/087,567 (2014年12月4日提交)、美国临时专利申请号62/087,571 (2014年12月4日提交) 和美国专利申请号14/802,675 (2015年7月17日提交) 的优先权,其中上述每者通过援引整体并入本文并且用于全部的目的。

技术领域

[0003] 本发明涉及吸入器、吸入监测系统和用于监测吸入器的方法。

背景技术

[0004] 吸入器或喷气器 (puffer) 被用于通过肺向身体递送药物。它们被用在例如治疗哮喘和慢性阻塞性肺病 (COPD) 中。吸入器的类型包括定量吸入器 (MDIs)、软雾吸入器 (Soft Mist Inhalers) (SMIs)、雾化器和干粉吸入器 (DPIs)。

[0005] 潮式吸入器是一类吸入器,其中药物以多次连续吸入 (例如它可被称为潮式呼吸) 而不是单次吸入被用掉。患者在静置呼吸模式 (at rest breathing pattern) 使用他们正常的呼吸而无需夸大的吸入流速 (还被称为用力吸入策略 (forced inhalation maneuver))。

[0006] 呼吸量计是用于测量通过患者肺吸入和呼出的空气的体积的仪器。呼吸量计测量换气,进入和流出肺的空气的移动。从由呼吸量计输出的踪迹 (被称为呼吸描记图), 鉴定异常的 (阻塞性的或限制性的) 换气模式是有可能的。现有的呼吸量计采用各种各样的不同测量方法,该方法包括压力传感器、超声波和液位表。

[0007] 最大流量计被用于测量最大呼气流量 (PEF) (还称为最大呼气流速 (PEFR))。这是一个人呼气的最大速度。PEF与通过细支气管的气流,和因此呼吸道中的阻塞程度相关。当呼吸道是收缩的 (例如由于肺部状况的恶化) 时,最大流量读数是较低的。从记录的数值的变化可以看出,患者和医生可测定肺功能、症状的严重性和治疗。最大流量计还被用于诊断。

[0008] 呼吸量计和最大流量计通常还被用于监测个体 (尤其遭受比如哮喘和COPD的状况的肺患者) 的肺功能和/或肺健康。根据呼气测量值比如PEF定义肺功能。

[0009] 肺功能的另一个测量值是1秒内用力呼气量 (FEV₁)。FEV₁是在充分吸气之后在1秒内用力喷出的空气的体积。在阻塞性疾病 (例如哮喘、COPD、慢性支气管炎、肺气肿) 中,由于对呼气流量增加的呼吸道阻力,减小了FEV₁。

[0010] 患者肺功能通常在与医师定期地会诊期间或响应症状的重现或加重时被监测。基于实践性原因,在明显的身体健康期间,监测典型地是相对罕见的。因此,反应性治疗并不总是被授予,一旦它理想上可以是,并且预防性治疗可以超过必要被使用。

[0011] 一些患者发现呼吸量计和最大流量计使用起来很复杂并且在他们的使用中也许需要培训和监督。由于这种问题并且基于成本的原因,大部分患者不具有个人呼吸量计或

最大流量计。

[0012] 对于具有阻塞性肺状况的患者来说,需要的是监测肺功能和/或健康的改进方式。

发明内容

[0013] 根据第一方面,本文提供了吸入监测系统,所述吸入监测系统包括:吸入器,所述吸入器包括经配置在使用者的吸入期间向使用者递送药物的药物递送仪器;吸入监测仪器,所述吸入监测仪器经配置在所述吸入期间采集用于确定使用者的肺功能和/或肺健康的测量值的数据;以及处理器,所述处理器经配置接收来自所述吸入监测仪器的所述数据并且使用所述数据确定使用者的肺功能和/或肺健康的测量值。

[0014] 该吸入器可以是干粉吸入器。该吸入器可以是加压定量吸入器(pMDI)。该吸入器可以是湿雾化器(wet nebuliser)。该吸入器可以是潮式吸入器。

[0015] 所述处理器能够经配置以通过从数据确定最大吸气流量(PIF)确定所述使用者的肺功能和/或肺健康的测量值。所述处理器能够经配置以通过从数据确定总的吸入量确定所述使用者的肺功能和/或肺健康的测量值。

[0016] 吸入监测系统能够进一步包括用户界面。此类用户界面能够经配置以向使用者提供所述使用者的肺功能和/或肺健康的测量值的指示。此类用户界面能够经配置以向照料者提供所述使用者的肺功能和/或肺健康的测量值的指示。此类用户界面能够经配置以向医学专家提供所述使用者的肺功能和/或肺健康的测量值的指示。

[0017] 所述指示可以包括绝对值。所述指示可以包括相对值。所述指示可以包括二元健康指标(binary health indicator)。所述指示可以包括测量值是否在安全区以上、以下或以内的三元指标。

[0018] 所述指示可以取决于与使用者相关的数据。

[0019] 该吸入监测系统可以进一步包括发射器。所述发射器可以是无线的。

[0020] 所述发射器能够经配置向使用者装置发送数据用于处理。所述发射器能够经配置向使用者装置发送数据用于存储。所述发射器能够经配置向使用者装置发送数据用于向使用者提供。所述发射器能够经配置向使用者装置发送数据用于向照料者提供。所述发射器能够经配置向使用者装置发送数据用于向医学专家提供。

[0021] 所述发射器能够经配置向服务器发送数据用于处理。所述发射器能够经配置向服务器发送数据用于存储。所述发射器能够经配置向服务器发送数据用于向使用者提供。所述发射器能够经配置向服务器发送数据用于提供给照料者。所述发射器能够经配置向服务器发送数据用于向医学专家提供。

[0022] 所述发送器能够经配置向数据云发送数据用于存储。

[0023] 所述发射器能够经配置向使用者装置发送所述测量值用于处理。所述发射器能够经配置向使用者装置发送所述测量值用于存储。所述发射器能够经配置向使用者装置发送所述测量值用于向使用者提供。所述发射器能够经配置向使用者装置发送所述测量值用于向照料者提供。所述发射器能够经配置向使用者装置发送所述测量值用于向医学专家提供。

[0024] 所述发射器能够经配置向服务器发送所述测量值用于处理。所述发射器能够经配置向服务器发送所述测量值用于存储。所述发射器能够经配置向服务器发送所述测量值用

于向使用者提供。所述发射器能够经配置向服务器发送所述测量值用于向照料者提供。所述发射器能够经配置向服务器发送所述测量值用于提供给医学专家。

[0025] 所述发射器能够经配置向数据云发送所述测量值用于存储。

[0026] 美国临时专利申请号62/011,808和62/135,798和美国专利申请号14/802,675(每者通过援引整体并入到本文中)描述了支持医疗装置和电子装置之间通信的接口装置。此类接口可以被利用在本文描述的吸入监测系统中。

[0027] 所述处理器能够被包括在所述吸入器中。所述吸入监测仪器能够被包括在所述吸入器中。所述吸入监测仪器能够经配置被连接到所述吸入器使得它与其流道气动连通。所述用户界面能够被包括在所述吸入器中。所述发射器能够被包括在所述吸入器中。

[0028] 所述吸入监测仪器能够包括压力传感器。所述压力传感器可以是微机电系统(MEMS)压力传感器(microelectromechanical system(MEMS) pressure sensor)。所述压力传感器可以是气压MEMS压力传感器。所述压力传感器可以是纳米机电系统(NEMS)压力传感器(nanoelectromechanical system(NEMS) pressure sensor)。

[0029] 所述吸入监测仪器能够经配置通过取样一系列时间点处的压力差或绝对压力采集数据。

[0030] 所述取样可以是定期的。所述取样周期可以是约50ms。取样频率可以是例如100Hz。

[0031] 所述药物递送仪器能够经进一步配置在继所述吸入之后的使用者的进一步吸入期间向使用者递送药物。该进一步吸入可以通过使用者使用潮式吸入器的新的呼吸或通过使用者使用例如干粉吸入器的第一次吸入的继续。

[0032] 所述吸入监测仪器能够进一步被配置在所述进一步吸入期间采集进一步的数据用于确定使用者的肺功能和/或肺健康的进一步测量值。所述处理器能够进一步被配置接收来自吸入监测仪器的所述进一步数据。所述处理器能够进一步被配置通过使用进一步数据确定使用者的肺功能和/或肺健康的进一步测量值。所述处理器能够进一步被配置比较数据和进一步数据。所述处理器能够进一步被配置比较使用者的肺功能和/或肺健康的测量值和所述使用者的肺功能和/或肺健康的进一步测量值。

[0033] 该处理器能够进一步被配置通过使用所述比较确定所述吸入器的使用功效。

[0034] 该处理器能够进一步被配置通过使用所述比较预测使用者的肺功能和/或肺健康的未来变化。

[0035] 所述使用者的肺功能和/或肺健康的未来变化可以包括目前的呼吸状况(比如哮喘或慢性阻塞性肺病(COPD))的恶化。

[0036] 该吸入监测系统能够经配置在响应所述处理器中向使用者提供警报,所述处理器预测一预定组的使用者的肺功能和/或肺健康的未来变化中的一个。该吸入监测系统能够经配置在响应所述处理器中向照料者提供警报,所述处理器预测一预定组的使用者的肺功能和/或肺健康的未来变化中的一个。该吸入监测系统能够经配置在响应所述处理器中向医学专家提供警报,所述处理器预测一预定组的使用者的肺功能和/或肺健康的未来变化中的一个。

[0037] 所述预测能够使用从受试者(而不是使用者)收集的数据。

[0038] 所述处理器能够经配置通过使用数学模型(比如回归模型)确定所述使用者的肺

功能和/或肺健康的测量值。

[0039] 所述数学模型可以属于总的吸入量和1秒内的用力呼气量(FEV₁)之间的关联性。所述数学模型可以属于最大吸气流量(PIF)和1秒内的用力呼气量(FEV₁)之间的关联性。所述数学模型可以属于总的吸入量和最大呼气流量(PEF)之间的关联性。所述数学模型可以属于最大吸气流量(PIF)和最大呼气流量(PEF)之间的关联性。

[0040] 对于多次吸入潮式吸入器或雾化器,所述数学模型属于1秒内的用力呼气量(FEV₁)和呼气流量变化的速率之间的关联性。

[0041] 对于单次吸入干粉吸入器,使用者的肺功能和/或肺健康的测量值可以基于使用者的单次呼吸。对于潮式吸入器或雾化器,该测量值可以基于使用者的多次呼吸。可以设想通过多次呼吸生成的无关的数据点可以被放弃,仅仅留下可用于数据处理的好的数据点。

[0042] 该数学模型可以考虑针对使用者的生物特征数据。

[0043] 所述生物特征数据可以包括性别。所述生物特征数据可以包括年龄。所述生物特征数据可以包括身高。所述生物特征数据可以包括体重。

[0044] 该吸入监测系统可以进一步包括用户界面装置,该用户界面装置能够打开和/或关闭所述药物递送仪器使得当该药物递送仪器被关闭时,所述吸入器可用作呼吸量计。

[0045] 所述用户界面装置可以包括吸入器的吸口盖子(mouthpiece cover)。所述吸口盖子可以被连接到药物递送仪器使得每当所述盖子被打开时,一剂药物可用于通过吸入器的吸口吸入。药物递送仪器可以被配置使得没有进一步剂量的药物可用于通过所述吸口吸入直至盖子已经再次完全地被关闭和打开。

[0046] 吸入监测系统可以进一步包括安慰剂吸入器装置(placebo inhaler device)。所述安慰剂吸入器装置可以包括所述吸入监测仪器。所述安慰剂吸入器装置可以被配置可行地连接到所述吸入监测仪器。所述安慰剂吸入器装置可以向使用者提供与所述吸入器大体上相同的吸入流阻。

[0047] 吸入监测系统可以包括经配置以向药物递送仪器提供电力的电池。吸入监测系统可以包括经配置向吸入监测仪器提供电力的电池。吸入监测系统可以包括经配置向处理器提供电力的电池。

[0048] 吸入监测系统可以进一步包括经配置存储数据的存储器。吸入监测系统可以进一步包括经配置存储所述测量值的存储器。

[0049] 吸入监测系统的药物递送仪器可以包括药物,和/或可以是包括吸入监测系统和药物的成套工具的一部分。药物可以包括一种或多种活性成分,例如长效毒蕈碱拮抗剂(muscarinic antagonist)(LAMA)、短效毒蕈碱拮抗剂(SAMA)、长效 β_2 -激动剂(LABA)、短效 β_2 -激动剂(SABA)和/或吸入皮质激素(ICS)中的一种或多种。

[0050] 根据第二方面,本文提供了一种方法,所述方法包括:使用吸入器在使用者的吸入期间向使用者递送药物;在所述吸入期间,采集数据用于确定使用者的肺功能和/或肺健康的测量值;以及使用该数据确定使用者的肺功能和/或肺健康的测量值。

[0051] 吸入器可以是干粉吸入器。吸入器可以是加压定量吸入器(pMDI)。吸入器可以是湿雾化器。吸入器可以是潮式吸入器。

[0052] 所述确定可以通过从数据确定最大吸气流量(PIF)做出。所述确定可以通过从数据确定总的吸入量做出。

[0053] 该方法可以进一步包括借助用户界面向使用者提供所述使用者的肺功能和/或肺健康的测量值的指示。该方法可以进一步包括借助用户界面向照料者提供所述使用者的肺功能和/或肺健康的测量值的指示。该方法可以进一步包括借助用户界面向医学专家提供所述使用者的肺功能和/或肺健康的测量值的指示。

[0054] 所述指示可以包括绝对值。所述指示可以包括相对值。所述指示可以包括二元健康指标。所述指示可以包括测量值是否在安全区以上、以下或以内的三元指标。

[0055] 所述指示可以取决于与使用者相关的数据。

[0056] 该方法可以进一步包括借助发射器向用户装置发送数据用于处理。该方法可以进一步包括借助发射器向用户装置发送数据用于存储。该方法可以进一步包括借助发射器向用户装置发送数据用于向使用者提供。该方法可以进一步包括借助发射器向用户装置发送数据用于向照料者提供。该方法可以进一步包括借助发射器向用户装置发送数据用于向医学专家提供。

[0057] 该方法可以进一步包括借助发射器向服务器发送数据用于处理。该方法可以进一步包括借助发射器向服务器发送数据用于存储。该方法可以进一步包括借助发射器向服务器发送数据用于向使用者提供。该方法可以进一步包括借助发射器向服务器发送数据用于向照料者提供。该方法可以进一步包括借助发射器向服务器发送数据用于向医学专家提供。

[0058] 该方法可以进一步包括借助发射器向数据云发送数据用于存储。

[0059] 该方法可以进一步包括借助发射器向用户装置发送所述测量值用于处理。该方法可以进一步包括借助发射器向用户装置发送所述测量值用于存储。该方法可以进一步包括借助发射器向用户装置发送所述测量值用于向使用者提供。该方法可以进一步包括借助发射器向用户装置发送所述测量值用于向照料者提供。该方法可以进一步包括借助发射器向用户装置发送所述测量值用于向医学专家提供。

[0060] 该方法可以进一步包括借助发射器向服务器发送所述测量值用于处理。该方法可以进一步包括借助发射器向服务器发送所述测量值用于存储。该方法可以进一步包括借助发射器向服务器发送所述测量值用于向使用者提供。该方法可以进一步包括借助发射器向服务器发送所述测量值用于向照料者提供。该方法可以进一步包括借助发射器向服务器发送所述测量值用于向医学专家提供。

[0061] 该方法可以进一步包括借助发射器向数据云发送所述测量值用于存储。

[0062] 所述发射器可以是无线发射器。

[0063] 正如以上所提到的,根据本发明的第二方面,本文提供了一种方法,所述方法包括:使用吸入器在使用者的吸入期间向使用者递送药物;在所述吸入期间,采集数据用于确定使用者的肺功能和/或肺健康的测量值;以及使用该数据,确定使用者的肺功能和/或肺健康的测量值。

[0064] 所述采集可以通过所述吸入器完成。所述确定可以通过所述吸入器做出。

[0065] 所述采集可以通过吸入监测仪器完成。所述方法可以进一步包括连接所述吸入监测仪器到吸入器使得吸入监测仪器与吸入器的流道气动连通。

[0066] 所述用户界面可以被包括在所述吸入器中。所述发射器可以被包括在所述吸入器中。

[0067] 所述采集可以借助压力传感器进行。所述压力传感器可以是微机电系统 (MEMS) 压力传感器。所述压力传感器可以是气压MEMS压力传感器。所述压力传感器可以是纳米机电系统 (NEMS) 压力传感器。

[0068] 所述数据采集可以包括取样在一系列时间点处的压力差。所述数据采集还可以包括取样在一系列时间点处的绝对压力。

[0069] 所述取样可以是定期的。

[0070] 所述取样周期可以是约50ms。取样频率可以是例如100Hz。

[0071] 该方法可以进一步包括在继所述吸入之后在使用者的进一步吸入期间向使用者递送药物。该方法可以进一步包括在所述进一步吸入期间,采集进一步数据用于确定使用者的肺功能和/或肺健康的进一步测量值。该方法可以进一步包括使用进一步数据确定使用者的肺功能和/或肺健康的进一步测量值。该方法可以进一步包括比较数据和进一步数据。该方法可以进一步包括比较使用者的肺功能和/或肺健康的测量值和所述使用者的肺功能和/或肺健康的进一步测量值。

[0072] 该方法可以进一步包括通过采用所述比较确定所述吸入器的使用功效。

[0073] 所述方法可以进一步包括通过采用所述比较预测使用者的肺功能和/或肺健康的未来变化。

[0074] 所述使用者的肺功能和/或肺健康的未来变化可以包括目前呼吸状况的恶化,该呼吸状况比如哮喘、慢性阻塞性肺病 (COPD)、呼吸道合胞体病毒 (RSV)、囊胞性纤维症 (CF)、特发性肺纤维化 (idiopathic pulmonary fibrosis) (IPF) 或肺栓塞 (PE)。

[0075] 该方法可以进一步包括在响应所述预测中向使用者提供警报。该方法可以进一步包括在响应所述预测中向照料者提供警报。该方法可以进一步包括在响应所述预测中向医学专家提供警报。

[0076] 所述预测可以采用从受试者 (而不是使用者) 收集的数据。

[0077] 所述使用者的肺功能和/或肺健康的测量值的所述确定可以使用数学模型。所述数学模型可以是回归模型。

[0078] 所述数学模型可以属于总的吸入量和1秒内的用力呼气量 (FEV₁) 之间的关联性。所述数学模型可以属于最大吸气流量 (PIF) 和1秒内的用力呼气量 (FEV₁) 之间的关联性。所述数学模型可以属于总的吸入量和最大呼气流量 (PEF) 之间的关联性。所述数学模型可以属于最大吸气流量 (PIF) 和最大呼气流量 (PEF) 之间的关联性。

[0079] 数学模型可以考虑针对使用者的生物特征数据。

[0080] 所述生物特征数据可以包括性别。所述生物特征数据可以包括年龄。所述生物特征数据可以包括身高。所述生物特征数据可以包括体重。

[0081] 该方法可以进一步包括:关闭吸入器的药物递送功能;以及使用作为呼吸量计的吸入器。

[0082] 对于单次吸入干粉吸入器,例如,关闭所述药物递送功能可以包括打开吸入器的吸口盖子。所述盖子可以经配置使得每当盖子被打开时,一剂药物通过吸入器的吸口可用于吸入。吸入器可以经配置使得没有进一步剂量的药物可用于通过吸口吸入直至盖子已经再次完全地被打开和关闭。

[0083] 该方法可以进一步包括使用安慰剂吸入器装置。

[0084] 所述采集可以通过吸入监测仪器进行。所述安慰剂吸入器装置可以包括所述吸入监测仪器。所述安慰剂吸入器装置可以经配置可行地连接到所述吸入监测仪器上。

[0085] 所述安慰剂吸入器装置可以向使用者提供与所述吸入器大体上相同的吸入流阻。对于多次吸入潮汐吸入器或湿雾化器(其也许具有比干粉吸入器更低的吸入流阻),使用具有定义的吸入流阻的特定的非药物套筒(non-drug cartridge)也许是有优势的。非药物套筒可以通过相同手段(其被用于识别套筒内的药物),例如通过电可擦可编程序只读存储器,电子地识别其本身为吸入器。

[0086] 该方法可以进一步包括将数据和/或所述测量值存储在存储器。

[0087] 附图的简要描述

[0088] 现在参照附图,借助实例描述本发明的各方面。在附图中:

[0089] 图1a说明了在吸入期间PEF和测量的最大流量之间的例示关联性;

[0090] 图1b说明了FEV1和总的吸入量之间的例示关联性;

[0091] 图2图示地说明了例示的吸入监测系统;以及

[0092] 图3是例示的吸入监测方法的流程图。

[0093] 详细描述

[0094] 以下描述被提供以使得本领域技术人员能够制作和使用该系统并且被提供在特定应用的上下文中。公开的实施方案的各种修改对本领域技术人员来说是显而易见的。

[0095] 本文定义的一般性原理可以应用于其它的实施方案和应用而没有脱离本发明的精神和范围。因此,本发明没有局限于显示的实施方案,但与本文公开的原理和特征一致的最宽范围一致。

[0096] 许多肺患者规定使用吸入器,使得他们或照料者能够向他们投予药物作为常规的预防措施以减轻恶化或两者。此类患者和照料者在使用这些吸入器中被培训并且对它们很熟悉。因此,推荐通过使用他们的吸入器监测患者的肺功能。监测肺健康同时投予药物减少了患者、照料者和医学专家管理肺状况所需要的时间和努力。

[0097] 这是之前没有考虑到的,因为正如以上所解释的,肺功能通常通过采用呼气测量值评估并且例如干粉吸入器通常不被设计允许呼气。在一些情况下,例如一些干粉吸入器,进入吸入器的呼气会削弱它们的功能(例如,如果来自呼气的水分引起粉末状的药物形成块,甚至使得投予更加困难)。

[0098] 然而,申请人已经建立肺功能的一些呼气测量值和一些吸气测量值之间的关联性。例如,参见图1a,该图显示了PEF和吸入期间测量的最大流量(最大吸气流量,PIF)之间的关联性和图1b,该图显示了FEV1和总的吸入量之间的关联性。回归线和它们的方程式被显示在图上,其中:

[0099] x_1 = 性别(男性=0;女性=1)

[0100] x_2 = 年龄/年

[0101] x_3 = 身高/cm

[0102] x_4 = 体重/kg

[0103] x_5 = PEF/ $l \cdot \min^{-1}$

[0104] x_6 = FEV1/ $l \cdot \min^{-1}$

[0105] y_1 = 吸入量/l

[0106] $y_2 = PIF/1$

[0107] 因此,建议处理采集的吸入数据,同时用吸入器投予药物以确定肺功能和/或健康。

[0108] 图2图示地说明了例示的吸入监测系统200。吸入器210包括药物递送仪器211。例如,这可以如同PCT专利申请公开号W0 01/97889、W0 02/00281、W0 2005/034833或W0 2011/054527中任意一者描述的干粉吸入器,这些PCT专利申请整体并入到本文中。吸入监测系统还可包括其它类型的吸入器/雾化器,例如加压定量吸入器(pMDIs)或湿雾化器。该吸入器要求用力吸气策略或仅仅潮式呼吸。

[0109] 吸入监测仪器220还可以被包括在所示的吸入器中或可以被包括在与它连接的分立单元中。吸入监测仪器例如包括如美国专利申请号62/043,126 (Morrison)、62/043,120 (Morrison)和62/043,114 (Morrison)中任意一者描述的微型,例如微机电、MEMS或纳米机电、NEMS)压力传感器,这些美国专利申请整体并入到本文中。其它合适的配置能够被设想。对于那些利用压力传感器的配置,所述传感器应当与吸入器的气流通道(通过该气流通道,使用者吸气)气动连通。

[0110] 为了确定使用者的肺功能和/或健康的测量值,处理器230与吸入监测仪器通信以处理由吸入监测仪器收集的数据。该处理器可以被包括在所示的吸入器中或如果吸入监测仪器被包括在分立辅助单元中,处理器还可以被包括在所述辅助单元中。如果吸入监测仪器配备有有线或无线发射器221,处理器可以在分立装置中,例如用户装置比如智能手机、平板电脑、笔记本电脑或PC。如果吸入监测仪器配备有能够与比如因特网的网络通信的发射器,该处理能够远程地完成,例如在医学专家的PC或在公共医疗卫生服务、吸入器制造商或云服务器上。例如,上述提到的装置或服务中的任意一者还被用于数据储存。处理器230可以由在上述提到的位置中任意一者的多个处理器组成,例如一些基本的处理可以在船上的吸入器完成,同时更多详细的分析被卸载到远程的装置或服务上。

[0111] 吸入器可以包括用户界面240用来提供与吸入器的使用和/或确定的肺功能和/或肺健康相关的信息。例如这可以是屏幕、指示灯、指示器蜂鸣器、扬声器、传统剂量计数带子(traditional dose counter tape)、振动警报等或这些或类似的任意组合。可替代地或另外,此类信息可以通过一个或多个患者或照料者或医学专家的用户装置的用户界面提供。

[0112] 该系统还可以包括用于存储收集的数据、计算结果和用于处理器执行的计算机代码指令的存储器250。正如处理器,存储器可位于吸入器或外部装置或服务中。

[0113] 吸入器的电子元件可以由电池212提供电力使得吸入器可以是便携式的

[0114] 该吸入器可以进一步包括用于将药物递送仪器置于运转或不运转的切换工具。当药物递送仪器不起作用时,吸入器可以被用作呼吸量计。作为一个实例,如果药物递送仪器处于电子(例如按钮操作的)控制下,电子切换工具可以被提供。作为另一个实例,PCT专利申请公开号W0 2005/034833(其通过援引整体并入到本文中)描述了用于计量干粉吸入器的机构,其中计量杯从料斗测量出一剂药物并且通过连接到吸口盖子的轭的作用被移动到给药位置。因此,打开吸口盖子使得吸入器准备好使用并且一旦一剂量已经被吸入,进一步给药是不可能的直到盖子已经再次被关闭和打开。使用此类具有本文推荐的吸入监测仪器的吸入器,患者能够服用他们剂量的药物,并且在关闭吸口盖子之前,通过吸口做出一个或多个进一步吸入用于进一步数据收集的目的。这允许更大量的数据被收集而没有让患者冒

药量过多的风险。作为另外一个实施例,呼吸量计套筒可被连接到可替换的套筒潮式吸入器并且患者能够通过呼吸量计套筒做出一个或多个进一步吸入用于进一步数据收集的目的。

[0115] 可替换地或此外,上述描述的吸入器可被提供在具有安慰剂或虚拟吸入剂的成套工具中,其具有类似真实吸入器的流阻,但它也不包括药物递送仪器,是空的或装有安慰剂物质比如乳糖。该安慰剂吸入器可以包括类似上述描述的吸入监测仪器的吸入监测仪器或可连接到此类仪器。

[0116] 如果吸入器210是例如湿雾化器,那么所有的电子元件可位于模块中,该模块可移除地连接到吸入端口为了避免电子器件暴露于流体。该模块可经配置被连接到具有变化的形状和尺寸的不同湿雾化器上。该模块可以包括具有定义的吸入流阻的流道,该定义的吸入流阻比单独湿雾化器(例如没有模块)的吸入流阻高。

[0117] 图3是例示的吸入监测方法300的流程图。在310,吸入(通过吸入器)开始。在320,药物通过吸入器递送。在330,涉及所述吸入的数据被收集。在340,吸入结束。在350,数据经处理以确定肺功能和/或肺健康的测量值。步骤320和330的顺序可以被颠倒或它们能够部分或完全地同时实施。步骤350可以在340之前、期间或之后并且在320之前、之后或完全或部分地与320同时发生。

[0118] 该数据还被用于由医师依从性监测例如以保证吸入器由使用者适当地使用。

[0119] 该处理可以包括使用数学模型比如图1中说明的回归模型。

[0120] 每当吸入器被使用时,方法300可以被重复,例如它可以是每天的。从多次使用吸入器采集的数据和/或从该数据做出的确定可以被储存并且经比较以提供一段时间的状况的进展的指示。该信息可被用于确定当前治疗方案的功效并且通知可能被要求的任何变化。该处理器还能够使用数据和/或确定以预测肺功能和/或肺健康的未来变化。该预测可以基于从正在讨论中的患者(patient in question)收集的数据(例如仅仅基于数据),和/或还能并入从其它患者收集的数据。例如,来自如上所描述的许多吸入器的使用者的数据可以被整理并且被用于鉴定在特定肺状况的恶化之前的吸入数据变化的模式。因此,处理逻辑可以是自主学习的。如果特定的患者数据然后被观察到匹配此类模式的开始,他们或他们的照料者或医师可以被警告使得治疗方案的任意要求的变化(例如增加的剂量、额外的药物或疗法)可以被做出以帮助避免恶化。

[0121] 通过吸入监测仪器收集的数据例如可以是压力差测量值或绝对压力测量值的时间系列。测量值可以定期地(例如在例如2、5或10秒内的每隔10ms、50ms或100ms)被获得。数据收集可以被重新设置在吸入监测仪器的使用之间。

[0122] 该用户界面可以提供,例如测量的PIF、计算的总的吸入量、计算的PEF、计算的FEV1的数值或相对于特定患者的理想值的这些数值中的一个的分数或百分比(例如所述理想值可以基于生物特征数据比如年龄、性别、身高、体重等选择)。可替换地或另外,它可以提供关于测量的数值是否在健康范围内的二元指标或关于测量的数值是否在健康范围以下、以上或以内的三元指标。此类健康范围的界限可以再次取决于针对特定的患者存储的生物特征数据。可替换地或另外,该用户界面可被用于指示服用的剂量数量或残留在一次性吸入器、可再装的料斗或一次性套筒的剂量数量。另一个可替换的或其它的指示可以是吸入器是否已经正确地使用,例如,使得患者或照料者或医学专家被警告漏服的剂量,对于

有效药物投予很不足或太弱的吸入,或药物已经不正确地被服用的吸入,和/或接收药物已经正确地服用的确认。

[0123] 吸入器优选地针对呼吸障碍(比如哮喘和/或COPD)的治疗。一系列种类的药物已经被开发以治疗呼吸障碍并且每类具有不同的目标和效果。

[0124] 支气管扩张药被利用以扩大支气管和细支气管,降低呼吸道阻力,从而增加对肺的气流。支气管扩张药可以是短效的或长效的。典型地,短效支气管扩张药提供了严重的支气管狭窄的快速减轻,然而长效支气管扩张药促进控制和预防更长期的症状。

[0125] 不同种类的支气管扩张药靶向呼吸道中的不同受体。两个常规使用的种类是抗胆碱能的药物(anticholinergics)和 β_2 -激动剂。

[0126] 抗胆碱能的药物(或“抗毒蕈碱的药物”(“antimuscarinics”))通过选择性地阻止神经细胞中它的受体阻止神经递质乙酰胆碱(neurotransmitter acetylcholine)。在局部施用,抗胆碱能的药物主要对位于呼吸道中的M3毒蕈碱型受体其起作用以产生平滑肌松弛,因此产生支气管扩张作用(bronchodilatory effect)。长效毒蕈碱拮抗剂(LAMAs)的优选实例包括噻托溴铵(溴化物)、氧托溴铵(oxitropium)(溴化物)、阿地溴铵(aclidinium)(溴化物)、异丙托铵(ipratropium)(溴化物)、格隆铵(glycopyrronium)(溴化物)、奥昔布宁(oxybutynin)(盐酸盐或氢溴酸盐)、托特罗定(tolterodine)(酒石酸盐)、曲司氯胺(trospium)(氯化物)、索利那新(solifenacin)(琥珀酸盐)、弗斯特罗定(fesoterodine)(延胡索酸盐)和达非那新(darifenacin)(氢溴酸盐)。在每种情况下,特别优选的盐/酯形式被指示在括号中。短效毒蕈碱拮抗剂(SAMAs)的优选实例包括托品酰胺(tropicamide)和环戊通(cyclopentolate)。

[0127] β_2 -肾上腺素能激动剂(或“ β_2 -激动剂”)对 β_2 -肾上腺素受体(β_2 -adrenoceptors)起作用,其引起平滑肌松弛,导致支气管通道的扩张。优选的长效 β_2 -激动剂(LABAs)包括福莫特罗(formoterol)(延胡索酸盐)、沙美特罗(salmeterol)(沙美特罗)(xinafoate)、茛达特罗(indacaterol)(马来酸盐)、班布特罗(bambuterol)(盐酸盐)、克仑特罗(clenbuterol)(盐酸盐)、奥达特罗(olodaterol)(盐酸盐)、卡莫特罗(carmoterol)(盐酸盐)、妥洛特罗(tulobuterol)(盐酸盐)和维兰特罗(vilanterol)(三乙酸苯酯)(triphenylacetate)。短效 β_2 -激动剂(SABAs)的实例包括柳丁氨醇(硫酸盐)、特布他林(terbutaline)(硫酸盐)、吡布特罗(pirbuterol)(醋酸盐)、奥西那林(metaproterenol)(硫酸盐)和沙丁胺醇(albuterol)。在每种情况下,特别优选的盐/酯形式被指示在括号中。

[0128] 用于治疗呼吸障碍的另一类药物是吸入皮质激素(ICSs)。ICS是用于长期控制呼吸障碍的类固醇激素。它们通过减少呼吸道炎症起作用。优选的实例包括布地奈德(budesonide)、倍氯米松(beclomethasone)(二丙酸盐)、氟替卡松(fluticasone)(丙酸盐或糠酸盐)、莫米松(mometasone)(糠酸盐)、环索奈德(ciclesonide)和地塞米松(dexamethasone)(钠)。在每种情况下,特别优选的盐/酯形式被指示在括号中。

[0129] 活性成分可以组合被投予,以及组合疗法和组合产品已经被推荐。公开在现有技术中的组合治疗和产品的实例被陈述在W0 2004/019985、W0 2007/071313、W0 2008/102128和W0 2011/069197中。活性成分可以是LAMA、LABA和ICS的组合。它们可以是LAMA和LABA、LAMA和ICS、LABA和ICS和/或诸如此类的双重组合。它们还可以是LAMA、LABA和ICS的组合。

[0130] 例示性组合是：

[0131] 奥昔布宁(盐酸盐或氢溴酸盐)和福莫特罗(延胡索酸盐)

[0132] 达非那新(氢溴酸盐)和福莫特罗(延胡索酸盐)

[0133] 奥昔布宁(盐酸盐或氢溴酸盐)、福莫特罗(延胡索酸盐)和倍氯米松(二丙酸盐)

[0134] 达非那新(氢溴酸盐)、福莫特罗(延胡索酸盐)和倍氯米松(二丙酸盐)

[0135] 奥昔布宁(盐酸盐或氢溴酸盐)和沙美特罗(salmeterol)(沙美特罗(xinafoate))

[0136] 达非那新(氢溴酸盐)和沙美特罗(salmeterol)(沙美特罗(xinafoate))

[0137] 奥昔布宁(盐酸盐或氢溴酸盐)、沙美特罗(salmeterol)(沙美特罗(xinafoate))
和氟替卡松(丙酸盐)

[0138] 达非那新(氢溴酸盐)、沙美特罗(salmeterol)(沙美特罗(xinafoate))
和氟替卡松(丙酸盐)

[0139] 格隆铵(溴化物)和茛达特罗(马来酸盐)

[0140] 格隆铵(溴化物)和福莫特罗(延胡索酸盐)

[0141] 噻托溴铵(溴化物)和福莫特罗(延胡索酸盐)

[0142] 噻托溴铵(溴化物)和卡莫特罗(盐酸盐)

[0143] 噻托溴铵(溴化物)和奥达特罗(olodaterol)(盐酸盐)

[0144] 噻托溴铵(溴化物)和茛达特罗(马来酸盐)

[0145] 布地奈德和福莫特罗(延胡索酸盐)

[0146] 在配制这些种类的活性成分用于通过吸入递送(比如通过干粉吸入器(DPI)、加压定量吸入器(pMDI)或雾化器)的过程中,许多方法已经被采取。

[0147] 药物的API应当深入地渗透到肺中以到达它们的作用位点。因此,APIs经微粒化以获得具有要求尺寸的颗粒,通常质量中位数气体动力学直径(mass medium aerodynamic diameter)(MMAD)为1-5 μ m。

[0148] 药物可以作为纯碎的药物被递送,但更合适地,优选药物连同赋形剂(载体)一起递送,该赋形剂适合吸入。合适的赋形剂包括有机赋形剂,比如多糖(例如淀粉、纤维素等)、乳糖、葡萄糖、甘露醇、氨基酸和麦芽糖糊精,以及无机赋形剂比如碳酸钙或氯化钠。乳糖是优选的赋形剂。

[0149] 粉末状药物和/或赋形剂的颗粒可以通过传统技术例如通过微电离作用(micronisation)、研磨或筛选制成。

[0150] 另外,药物和/或赋形剂粉末可以被设计具有特定的密度、尺寸范围或特征。颗粒可以包括活性剂、表面活性剂、壁形成材料或由本领域技术人员认为是需要的其它成分。

[0151] 药物可以被包含到吸入器的容器中或被放置在吸入器的内部的筒中。或者,药物可以分别地被提供给吸入器,例如以铝塑泡罩包装的单位剂量(in a blister strip of unit doses)或胶囊,其可以形成具有吸入器的成套工具部件。

[0152] 申请人在此独立地公开了本文描述的每个单独特征和两个或以上此类特征的任意组合,在这样的范围内,基于作为整体的本申请说明书,根据本领域技术人员的公知常识,此类特征或组合能够被实施,不考虑此类特征或特征的组合是否解决本文公开的任何问题并且不限于权利要求书的范围。申请人表明了本发明的各方面可以包括任何此类单个特征或特征的组合。根据上述描述,对本领域技术人员来说,各种修改可以在本发明的范围

内做出是显而易见的。

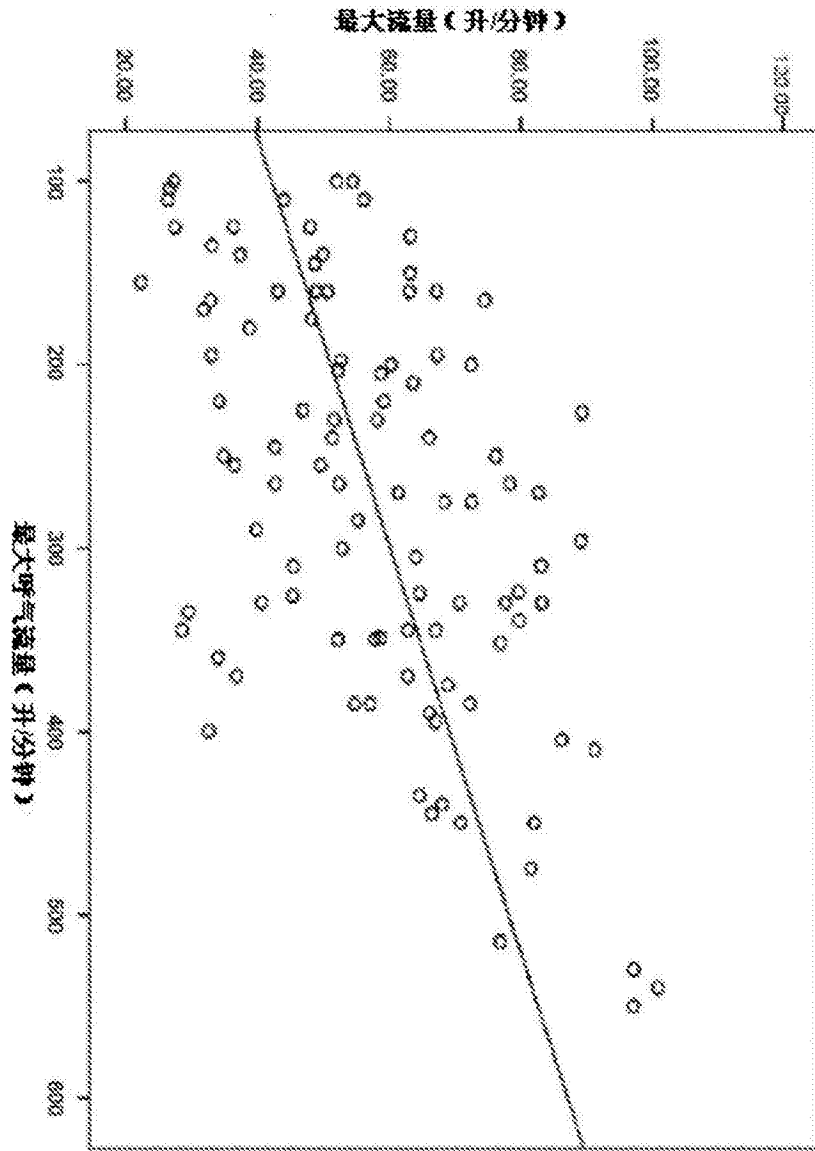


图1A

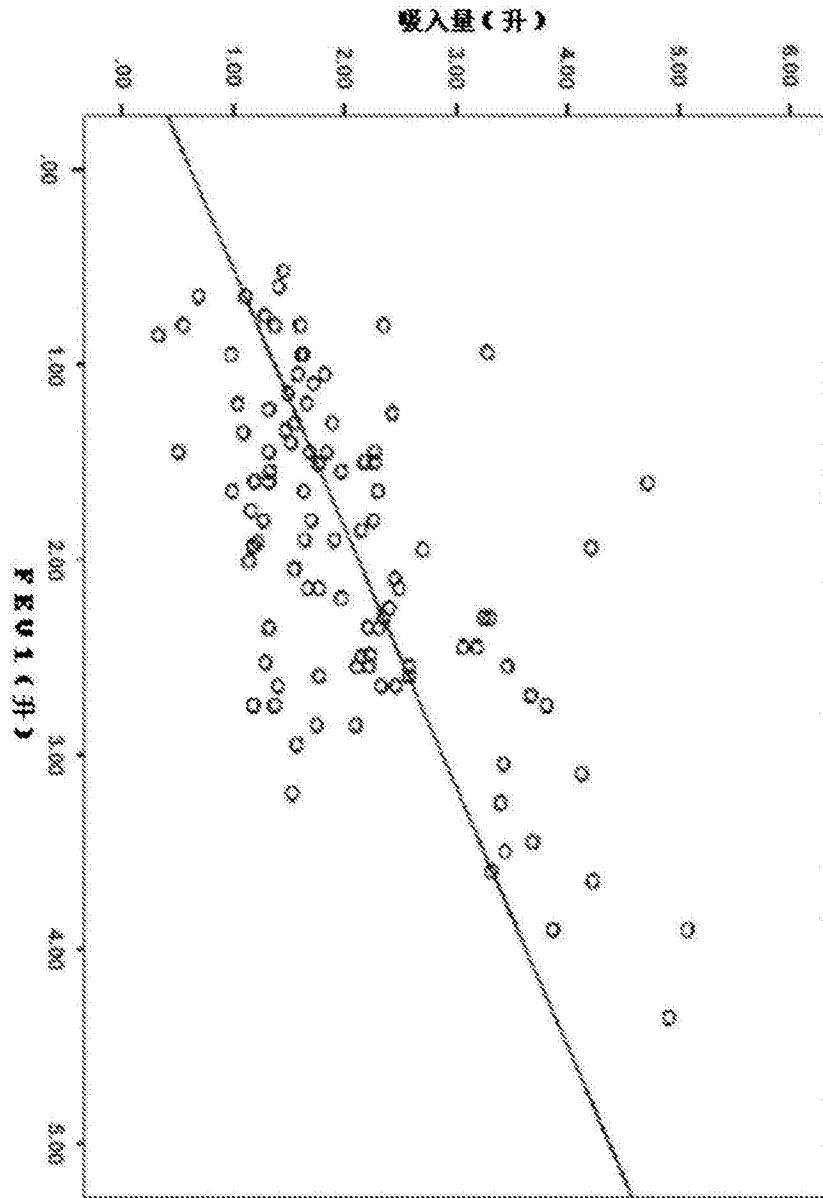


图1B

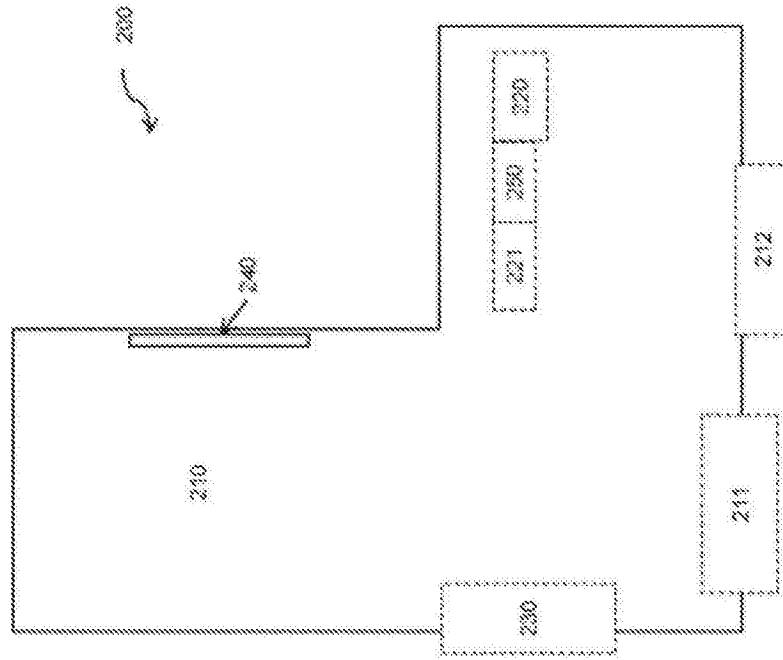


图2

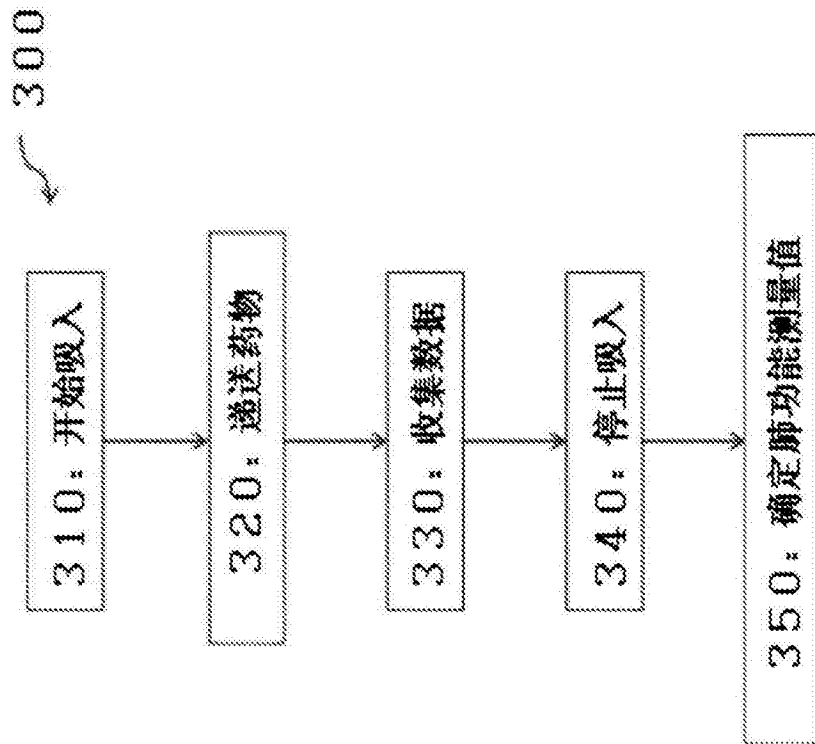


图3